WEST Search History

DATE: Wednesday, June 04, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT; PLUR=YES; OP=AND			
L1	fsh.clm. or lh.clm. or hlh.clm. or hcg.clm.	665	L1
L2	L1 and (silas$ or isoform$ or posttranslation$ or post-translation$ or iso-form$ or menopaus$ or postmenopaus$ or premenopaus$ or ovulat$)	178	L2
L3	L1 and (silas$ or isoform$ or posttranslation$ or post-translation$ or iso-form$ or menopaus$ or postmenopaus$ or premenopaus$ or ovulat$).clm.	35	L3
L4	premenopaus$ same postmenopaus$	165	L4
L5	premenopaus$.clm. same postmenopaus$.clm.	2	L5
L6	l4 same (hcg or lh or hlh or fsh or hfsh or gnrf)	4	L6
L7	L6 not l5	3	L7
L8	acid$ same fsh	514	L8
L9	acid$ near25 (fsh or follicle)	473	L9
L10	L9 same basic$	17	L10
L11	sialya$.clm.	3	L11
L12	sialyl$.clm.	190	L12
L13	L12 and gonad$	20	L13
L14	(method or process).clm. same menopaus$.clm.	268	L14

L15	(method or process).clm. same ($menopaus$).clm.	338	L15
L16	l15 and (fsh or lh or hcg or hhcg or rhcg or gonad$)	127	L16
L17	l15 and (fsh or lh or hcg or hhcg or rhcg or gonad$).clm.	26	L17
L18	iso-form or isoform	5499	L18
L19	L18 near25 (differentiat$ or determin$ or distinguish$ or heterogenous$)	707	L19
L20	L18 near25 (differentiat$ or determin$ or distinguish$)	707	L20
L21	L20 same (lh or fsh or hcg)	2	L21
L22	l18 near5 (lh or hcg or fsh or hormore)	13	L22
L23	l18 near5 (lh or hcg or fsh or hormone)	59	L23
L24	L18 near25 (hybridoma or mab or moab or monoclonal or mono-clonal)	242	L24
L25	L24 and (ovulat$ or preg$ or follicle or hlh or lh or fsh or hcg or female or menopause or premenopause or postmenopause or menopausal)	130	L25

END OF SEARCH HISTORY

Interpretations of five monoclonal **immunoassays of lutropin and follitropin: effects of normalization with WHO standard.**

Vermes I; Bonte H A; v d Sluijs Veer G; Schoemaker J
Department of Clinical Chemistry, Medisch Spectrum Twente, Enschede, The Netherlands.

Clinical chemistry (UNITED STATES) Mar 1991, 37 (3) p415-21, ISSN 0009-9147 Journal Code: 9421549
Comment in Clin Chem. 1991 Mar;37(3) 311-2; Comment in PMID 2004435
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Five mono(oligo)clonal immunometric assays for lutropin (LH) and follitropin (**FSH**)--bioMerieux, IRE-Medgenix, Serono Diagnostics, Diagnostics Products Corp. (DPC), and LKB--were evaluated in comparison with two polyclonal RIAs (DPC and Amersham). Detection limits varied from 0.04 to 0.32 int. unit/L and 0.06 to 0.86 int. unit/L for LH and **FSH** , respectively. Intra- and interassay precision (CV) at three concentrations varied from 2.0% to 29.8%, showing that not all kits tested gave acceptable results, especially for LH. Linearity and parallelism were acceptable, except for the DPC **FSH** kit and the bioMerieux LH kit. High-dose "hook" effects were seen in some kits at LH concentrations of 250 int. units/L, but not in the **FSH** kits up to concentrations of 350 int. units/L. Reagents in some kits cross-reacted with choriogonadotropin. The clinical validity of the assays was tested in 25 pre- and 25 postmenopausal healthy women and in 66 patients with polycystic ovary disease. In contrast to **FSH** , LH values varied significantly not only between polyclonal and **monoclonal** assays but also between the various **monoclonal** assays, despite the fact that all manufacturers state that their kits are calibrated on the same standards: WHO International Reference Preparation (IRP) 68/40 for LH and 78/549 for **FSH** . We normalized the results by using new WHO standards: IRP 80/552 for LH and IRP 83/575 for **FSH** . This decreased significantly the between-kit differences in LH results for individuals. The much-used LH/ **FSH** ratio greater than 3 for diagnosing patients with polycystic ovary disease is not valid when **monoclonal** assays are used, and is kit-dependent. However, using the normalized results yields a "new" LH/ **FSH** ratio, which is kit-independent and differs significantly between patients and healthy subjects.

Tags: Comparative Study; Female; Human
Descriptors: **Follicle Stimulating Hormone** --blood--BL; *LH--blood--BL; *Radioimmunoassay--methods--MT; Adolescence; Adult; Immunoradiometric Assay --methods--MT; **Menopause** --blood--BL; Polycystic Ovary Syndrome--blood--BL ; Reagent Kits, Diagnostic; Reference Standards
CAS Registry No.: 0 (Reagent Kits, Diagnostic); 9002-67-9 (LH); 9002-68-0 (Follicle Stimulating Hormone)
Record Date Created: 19910424

Descriptors: **Luteinizing Hormone** --pharmacokinetics--PK; * **Luteinizing Hormone** --pharmacology--PD; Biological Assay; Chromatography, High Pressure Liquid; Glycosylation; Half-Life; Leydig Cells--drug effects--DE; Leydig Cells--metabolism--ME; **Luteinizing Hormone** --analogs and derivatives--AA; **Luteinizing Hormone** --isolation and purification--IP; Metabolic Clearance Rate; Mice; N-Acetylneuraminic Acid--analysis--AN; Pituitary Gland, Anterior--chemistry--CH; Rats; Rats, Sprague-Dawley; Regression Analysis; Testosterone--blood--BL; Testosterone--metabolism--ME

CAS Registry No.: 131-48-6 (N-Acetylneuraminic Acid); 57-85-2 (Testosterone); 9002-67-9 (Luteinizing Hormone)

Record Date Created: 19961217

Record Date Completed: 19961217

14/9/10

DIALOG(R)File 155:MEDLINE(R)

10697361 97046607 PMID: 8891528

Glycosylation is the structural basis for changes in polymorphism and immunoreactivity of pituitary glycoprotein hormones.

Zerfaoui M; Ronin C

UPR 9024 CNRS, Marseille, France.

European journal of clinical chemistry and clinical biochemistry : journal of the Forum of European Clinical Chemistry Societies (GERMANY) Sep 1996, 34 (9) p749-53, ISSN 0939-4974 Journal Code: 9105775

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Glycoprotein hormones have long been known to display extensive polymorphism and changes in bioactivity according to the endocrine status of the patient. Structural analysis has shown that pituitary **gonadotropins** (lutropin and follitropin) and thyrotropin are synthesized and secreted as a panel of **isoforms** which differ in glycosylation, bioactivity and circulatory half-life. Ultrasensitive immunoassays could reveal that glycosylation of plasma hormones is structurally different from the pituitary stock so that the ratio of circulating glycoforms may vary according to the physiopathology of the pituitary axis. However, contradictory results between immunoassays have been often reported, suggesting that some plasma forms can escape recognition by monoclonal antibodies which have been raised to the pituitary or urinary antigen. When hormone levels do not correlate with clinical features, one can also suspect that inactive or hyperactive forms are being measured. At the molecular level, very limited information has been gained toward the expression of hormone epitopes as a function of carbohydrate structure. To address this issue, we have compared the recognition of pituitary and recombinant human thyrotropin by various polyclonal and monoclonal antibodies before and after neuraminidase treatment. Both, pituitary and recombinant thyrotropin bound to anti-alpha and anti-beta antibodies, demonstrating thereby that recombinant thyrotropin can be used to calibrate immunoassays. While removal of **sialic** acid did not alter the recognition of the recombinant hormone in various immunoassays, this treatment specifically abolished the binding of pituitary thyrotropin to anti-beta monoclonal antibodies. These findings show that immunoreactivity of circulating hormone glycoforms, which are often more **sialylated** than their pituitary counterparts, may very well account for variation depending on the antibodies used in the immunoassays. (12 Refs.)

Tags: Human

Descriptors: *Pituitary Hormones--chemistry--CH; *Pituitary Hormones --genetics--GE; *Polymorphism (Genetics); Chorionic **Gonadotropin** --chemistry--CH; Chorionic **Gonadotropin** --genetics--GE; **Follicle Stimulating Hormone** --chemistry--CH; **Follicle Stimulating Hormone** --genetics--GE; Glycoproteins--chemistry--CH; Glycoproteins--genetics--GE; Glycosylation; Immunoassay; Isoelectric Focusing; **Luteinizing Hormone** --chemistry--CH; **Luteinizing Hormone** --genetics--GE; Pituitary Hormones --immunology--IM; Recombinant Proteins--chemistry--CH; Thyrotropin --chemistry--CH; Thyrotropin--genetics--GE

1999756 99445408 PMID: 10514553

Oestrogens regulate pituitary alpha2,3- sialyltransferase **messenger ribonucleic acid levels in the female rat.**

Damian-Matsumura P; Zaga V; Maldonado A; Sanchez-Hernandez C; Timossi C; Ulloa-Aguirre A

Department of Reproductive Biology, Instituto Nacional de la Nutricion Salvador Zubiran, Mexico.

Journal of molecular endocrinology (ENGLAND) Oct 1999, 23 (2) p153-65, ISSN 0952-5041 Journal Code: 8902617

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Follicle-stimulating hormone (FSH) is synthesized by the anterior pituitary gland in multiple molecular forms. Increased acidic/ **sialylated** FSH charge **isoforms** are associated with conditions characterized by a low oestrogen output. In the present study, we analysed the dynamics of the changes in mRNA levels of the enzyme Galbeta1,3[4]GlcNAc alpha2,3- **sialyltransferase** (2,3-STase) (one of the enzymes that incorporate **sialic** acid residues into the FSH molecule) in intact and ovariectomized rats. The anterior pituitaries of 4-day regularly cyclic adult female Wistar rats were obtained at 1000 h on the days of pro-oestrus (P), oestrus (O), dioestrus 1 (D1) and dioestrus 2 (D2), at 0200 h, 1400 h, 1800 h and 2200 h on D1, at 1800 h on day of O and at 1000 h after 7, 14, 21, 28 and 45 days of oophorectomy performed on the morning of P. Total RNA was isolated from each gland and the 2,3-STase levels were measured by Northern blot hybridization analysis employing a 346-base pair cDNA probe encoding for a non-conserved amino acid sequence of the catalytic domain of the enzyme. Maximal levels of the enzyme mRNA were detected at 1000 h on D1; thereafter, they progressively decreased by 60% during the ensuing 24 h, reaching the lowest concentration values (26% of the maximally observed level on D1) at 1000 h on day of P and remaining unchanged during the morning of O. Administration of the potent oestradiol receptor antagonist ICI 182,780 at 1000 h on D1 completely reverted the time-dependent decrease in 2,3-STase mRNA levels observed during the afternoon of D1, whereas oestradiol benzoate administered at 1000 h on day of O significantly reduced the enzyme mRNA levels (to 21% of the levels detected in vehicle-treated controls). In ovariectomized rats, the alpha2,3-STase mRNA progressively increased from day 21 to day 45 post castration. Administration of oestradiol benzoate on day 28 after oophorectomy significantly reduced the 2,3-STase mRNA levels (to 36% of the levels detected in vehicle-injected controls); ICI 182,780 partially counteracted this oestradiol-mediated effect. The dynamics of these changes in 2,3-STase mRNA levels partially correlated with changes in the relative abundance of the FSH charge **isoforms** separated by preparative chromatofocusing of anterior pituitary extracts, particularly in glands obtained during the morning of P and O. These data demonstrate for the first time that pituitary 2,3-STase is a hormonally-regulated enzyme and that the changes in transcription and/or stability of its mRNA may be involved, in part, in the post-translational processing of the FSH molecule during certain physiological conditions.

0568008 96379946 PMID: 8787959

Undetectable luteinizing hormone levels using a monoclonal **immunometric** assay .

Barbe F; Legagneur H; Watrin V; Klein M; Badonnel Y

Service de Biologie Medicale, Maternite Regionale, Nancy, France.

Journal of endocrinological investigation (ITALY) Nov 1995, 18 (10) p806-8, ISSN 0391-4097 Journal Code: 7806594

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Previous studies have shown wide discrepancies among the results obtained with different immunometric **assays** . We present five cases (out of 4000 women) whose plasma luteinizing hormone was not detected using a LH immunometric **assay** (LH Stratus Baxter) but was recognized by other kits. These cases concerned one 28-year-old woman presenting with infertility and four postmenopausal women. The LH Amerlite kit gave detectable but low results. The results obtained with the other kits were > 7 IU/l. FSH levels were > 7 IU/l. In one case, sera were taken before and after the **menopause** ; differences between the LH results increased. Discrepancies among LH **assay** kits have been attributed to variation both in standard curve calibration and in epitope specificity of the kit **monoclonal** antibodies. The Baxter kit might misrecognize some **isoforms** present in postmenopausal women. The present data illustrate the potential false results with such **immunoassays** in routine clinical laboratory testing. When undetectable LH results are not clinically explained or when disparities between LH and FSH are observed, we suggest using a second **methodology** or a bioassay if necessary. Improvement in LH **assays** and standardization might resolve the problem of discrepancies between the LH results.

Tags: Comparative Study; Female; Human

Descriptors: Antibodies, **Monoclonal** ; * **Immunoassay** -- **methods** --MT; * **Luteinizing Hormone** --blood--BL; Adult; False Negative Reactions; **Follicle Stimulating Hormone** --blood--BL; **Immunoassay** --statistics and numerical data--SN; Middle Age; Postmenopause; Reagent Kits, Diagnostic --statistics and numerical data--SN

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Reagent Kits, Diagnostic); 9002-67-9 (Luteinizing Hormone); 9002-68-0 (Follicle Stimulating Hormone)

Record Date Created: 19961021

Record Date Completed: 19961021

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File 155:MEDLINE(R)  1966-2003/Jun W1
       (c) format only 2003 The Dialog Corp.
*File 155: Medline has been reloaded and accession numbers have
changed.  Please see HELP NEWS 155.

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            8052  PREMENOPAUS?
           22771  POSTMENOPAUS?
     S27       0  S25 AND (PREMENOPAUS? OR POSTMENOPAUS?)
?ds

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S2      26212   R1-R2
S3      87343   R1-R18
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S5        733   S4 AND ISOFORM?
S6        310   S5 AND (DISTING? OR DIFFERENTI? OR IDENTIF? OR SEPARA? OR -
              MENOPAUS?)
S7        109   S6 AND (ASSAY? OR IMMUNOASSAY? OR EIA OR ELISA OR ELIZA OR
              METHOD?)
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S9         75   S7 NOT S8
S10        11   S9 AND (HYBRIDOM? OR MONOCLONAL?)
S11       263   S5/2000:2003
S12       470   S5 NOT S11
S13        27   S12 AND SIAL?
S14        27   S13 NOT S10
S15     26323   MENOPAUS?
S16    312426   REVIEW OR TUTOR?
S17      1089   S15 AND S16
S18       118   S17 AND (GONAD? OR FSH? OR LH?)
S19       114   S18 AND HUMAN?
S20        52   S19 AND (DETERMIN? OR MEASUR? OR DISTING? OR DIFFERENT? OR
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S22        53   S17 AND PREDICT?
S23         0   S22 AND MONOCLONAL?
S24         6   S17 AND MONOCLONAL?
S25      1536   (SIALIC? OR SIALYL?) (25N) (MOAB OR MAB OR MONOCLONAL OR A-
              NTIBOD?)
S26         1   S25 AND S15
S27         0   S25 AND (PREMENOPAUS? OR POSTMENOPAUS?)
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           26323  S15
           29610  SIAL?
     S28       5  S15 (10N) SIAL?
?t s28/9/all
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3 and beta 3 possess the full length of the polypeptide chains, with the same amino acid sequences as those of the corresponding LH subunits alpha and beta, respectively; and 2) subunits alpha 1 and alpha 2 are complexes of three polypeptides which are missing several N-terminal residues from subunit alpha 3. Conversely, subunits beta 1 and beta 2 lack the C-terminal two residues and one residue, respectively, of subunit beta 3. Renotropic activity was not detected in any of the dissociated subunits alone, but association of alpha 1-3 with beta 1-3 reconstituted the hormonal activity with different potencies. In particular, combination of subunits alpha 3 and beta 3 (alpha 3.beta 3) yielded a potent renotropic activity with weak **gonadotropic** activity. The carbohydrate composition of the purified preparation exhibiting renotropic activity differed from that of a reference oLH preparation, which possessed greater **gonadotropic** activity but was devoid of renotropic activity. Furthermore, renotropic activity was decreased after removal of **sialic** acid by treatment with neuraminidase. Thus, the oligosaccharide moieties as well as the amino acid sequences of the subunits may play an important role in the expression of renotropic activity in vivo, these effects over and above those arising from differential metabolic clearance. We conclude that pituitary renotropin represents a novel activity of a LH- **isoform** (s) and that the posttranslational (or the artificial, i.e. during preparation) modification of the constituent LH subunits may be responsible for modulation of renotropic activity as well as the intrinsic **gonadotropic** activity.

Tags: Animal; Male; Support, Non-U.S. Gov't

Descriptors: DNA--biosynthesis--BI; *Kidney--metabolism--ME; * **Luteinizing Hormone** --pharmacology--PD; Amino Acid Sequence; Amino Acids --analysis--AN; Carbohydrates--analysis--AN; Chromatography; Chromatography, High Pressure Liquid; Electrophoresis, Polyacrylamide Gel; **Glycoprotein Hormones, alpha Subunit**; Hydrogen-Ion Concentration; Kidney--drug effects --DE; **Luteinizing Hormone** --isolation and purification--IP; Molecular Sequence Data; Molecular Weight; Neuraminidase--metabolism--ME; Peptide Fragments; **Pituitary Hormones, Anterior** --isolation and purification--IP; **Pituitary Hormones, Anterior** --pharmacology--PD; Radioimmunoassay; Rats; Rats, Inbred Strains; Trypsin

CAS Registry No.: 0 (Amino Acids); 0 (Carbohydrates); 0 (Glycoprotein Hormones, alpha Subunit); 0 (Peptide Fragments); 0 (Pituitary Hormones, Anterior); 9002-67-9 (Luteinizing Hormone); 9007-49-2 (DNA)

Enzyme No.: EC 3.2.1.18 (Neuraminidase); EC 3.4.21.4 (Trypsin)

Record Date Created: 19880829

Record Date Completed: 19880829

14/9/25

DIALOG(R)File 155:MEDLINE(R)

05187147 86188076 PMID: 3008870

Isolation and characterization of three forms of luteinizing hormone from the pituitary gland of the horse.

Matteri R L; Papkoff H; Ng D A; Swedlow J R; Chang Y S

Biology of reproduction (UNITED STATES) Apr 1986, 34 (3) p571-8, ISSN 0006-3363 Journal Code: 0207224

Contract/Grant No.: HD-05722; HD; NICHD

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Three **isoforms** of equine luteinizing hormone (eLH-A, eLH-B and eLH-C) have been isolated from horse pituitary glands. Separation was achieved on the basis of charge heterogeneity by ion-exchange chromatography. These charge differences were apparent after final purification, as determined by electrophoretic mobility on polyacrylamide disc gels (RF = 0.14, 0.19 and 0.26 for eLH-A, -B and -C, respectively). Apparent size differences were also noted between the isohormones by gel filtration on Sephadex G-100. Ve/Vo ratios for eLH-A, -B and -C were 1.72, 1.54 and 1.47, respectively. All 3 **isoforms** were found to contain an equivalent amount of hexose (9.0-9.2%). Isohormones eLH-B and eLH-C, however, possess more **sialic**

acid than eLH-A (6.6-6.7%, vs. 4.5%). The eLH-A and eLH-B preparations contain a similar amount of hexosamine, which is slightly lower than the amount of eLH-C (8.8-9.1% vs. 11.2%). No differences were noted between the isohormones by rat Leydig cell LH bioassay, equine testis LH radioreceptor assay (RRA) or calf testis follicle-stimulating hormone (FSH) RRA. Slight, but nonsignificant, variations were noted between preparations in an eLH radioimmunoassay (RIA). Although chemical variations were detected between the eLH **isoforms** , no significant differences were observed in in vitro biological and immunological activities. The differences detected in **sialic** acid content raises the possibility that differences in in vivo clearance rates may exist.

Tags: Animal; Support, U.S. Gov't, P.H.S.

Descriptors: Horses--physiology--PH; * **Luteinizing Hormone** --isolation and purification--IP; Biological Assay; Carbohydrates--analysis--AN; Chromatography, DEAE-Cellulose; Electrophoresis, Polyacrylamide Gel; **Luteinizing Hormone** --immunology--IM; **Luteinizing Hormone** --metabolism --ME; Receptors, Cell Surface--metabolism--ME; Receptors, FSH; Receptors, LH; Structure-Activity Relationship

CAS Registry No.: 0 (Carbohydrates); 0 (Receptors, Cell Surface); 0 (Receptors, FSH); 0 (Receptors, LH); 9002-67-9 (Luteinizing Hormone)

Record Date Created: 19860603

Record Date Completed: 19860603

14/9/26

DIALOG(R)File 155:MEDLINE(R)

05159239 86160038 PMID: 3955145

An in vitro study of LH release, synthesis and heterogeneity in pituitaries from proestrous and short-term ovariectomized rats.

Baldwin D M; Highsmith R F; Ramey J W; Krummen L A

Biology of reproduction (UNITED STATES) Mar 1986, 34 (2) p304-15, ISSN 0006-3363 Journal Code: 0207224

Contract/Grant No.: HD-16994; HD; NICHD

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

It is known that acute ovariectomy (OVX) greatly attenuates the pituitary luteinizing hormone (LH) response to **gonadotropin** -releasing hormone (GnRH) in vitro. The present study evaluated possible quantitative and/or qualitative differences in the biosynthesis and secretion of LH in pituitaries from proestrous and acutely (72 h) OVX rats. Paired anterior pituitary glands were incubated for 4 h in a medium containing +/- 10 nM GnRH. Pituitary and secreted LH were measured by radioimmunoassay with differences in total LH (tissue plus medium) +/- GnRH being indicative of GnRH-stimulated LH synthesis. Qualitative changes in LH were evaluated by isoelectrofocusing (IEF). The results show that the major form of LH stored in and released from the pituitaries consisted of LH molecules with an isoelectric point (pI) in the alkaline pH range (alkaline LH), and a lesser amount (approximately 30%) of LH molecules in the acidic pH range (acidic LH). The ratio of alkaline/acidic LH observed in the pituitary and medium was similar in the proestrous and OVX groups, although the amount of alkaline and acidic LH release in response to GnRH was 2-3 times greater in the proestrous group. In both groups, the alkaline/acidic LH ratio of secreted LH was higher in the presence of GnRH than in its absence. Alkaline LH synthesis was increased by GnRH in both groups, with the response being greater in the proestrous than in the OVX group; GnRH-stimulated acidic LH synthesis was observed only in the proestrous group. In both groups, the amount of LH synthesized was about 60% of the amount released, which suggests that LH synthesis does not fully account for differences in GnRH-stimulated LH release. Treatment of pituitary extracts with neuraminidase decreased acidic LH, and proportionately increased alkaline LH. These results suggest that the quality of LH stored in and secreted from pituitaries of proestrous and OVX rats is similar, and that there is a preferential release of the major alkaline LH **isoform** in response to GnRH. The ovarian steroid environment, presumably estradiol,

proportionately increases the amount of alkaline and acidic LH released, and differentially affects the amounts of the various **isoforms** synthesized in response to GnRH. The charge heterogeneity of alkaline and acidic LH may be related to the **sialic** acid content of the LH molecule.
Tags: Animal; Female; Support, U.S. Gov't, P.H.S.
Descriptors: **Luteinizing Hormone** --metabolism--ME; *Pituitary Gland, Anterior--metabolism--ME; Isoelectric Point; **Luteinizing Hormone** --secretion--SE; Ovariectomy; Pituitary Gland, Anterior--secretion--SE; Proestrus; Rats; Time Factors
CAS Registry No.: 9002-67-9 (Luteinizing Hormone)
Record Date Created: 19860505
Record Date Completed: 19860505

14/9/27
DIALOG(R)File 155:MEDLINE(R)

04054410 83183615 PMID: 6840529
Pituitary gonadotropic **hormone from a chondrostean fish, starred sturgeon (Acipenser stellatus Pall.) III. Polymorphism.**
Kuznetzov A A; Goncharov B F; Burzawa-Gerard E
General and comparative endocrinology (UNITED STATES) Mar 1983, 49 (3) p364-74, ISSN 0016-6480 Journal Code: 0370735
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Four biologically active fractions of **gonadotropic** hormone (aci-GTH-A, -B, -C, -D) were isolated and purified from acetonized pituitaries of the starred sturgeon (Acipenser stellatus Pall.). Their separation was achieved by DEAE-cellulose chromatography. Disc-electrophoresis and especially isoelectric focusing in polyacrylamide gel showed that each fraction contained several components. Not less than 15 different components as a whole with isoelectric points ranging from 4.5 to 7.0 could be counted in four aci-GTH preparations. All these components were active in toad oocyte maturation test. Only two of four preparations (aci-GTH-A and -D) were practically free of common components. All aci-GTH preparations were shown to be homogeneous and identical by molecular weight, sedimentation coefficient, **sialic** acid content, and some immunological properties. N-terminal amino acid analysis revealed tyrosine and leucine in all aci-GTH preparations, with the only exception of aci-GTH-D that contained an additional polypeptide with N-terminal glycine. No differences in the spectra of aci-GTH **isoforms** were found when pituitary extract, newly purified or 3 years older hormone preparations were submitted to isoelectric focusing.
Tags: Animal; Comparative Study; Female; Male
Descriptors: Fishes--metabolism--ME; * **Gonadotropins** , Pituitary --isolation and purification--IP; *Pituitary Gland--analysis--AN; Biological Assay; Bufonidae; Chromatography, DEAE-Cellulose; Chromatography, Gel; Electrophoresis, Polyacrylamide Gel; **Gonadotropins** , Pituitary--pharmacology--PD; Isoelectric Focusing; Oocytes--drug effects --DE; Oocytes--growth and development--GD; Polymorphism (Genetics)
CAS Registry No.: 0 (Gonadotropins, Pituitary)
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10697360 97046606 PMID: 8891527

Interest of epitopic dissection in immunoanalysis of proteins and peptides: review **of theoretical and practical aspects.**

Niccoli P; Ferrand V; Lejeune P J; Carayon P

Laboratoire de Biochimie Endocrinienne et Metabolique, Institut National de la Sante et de la Recherche Medicale, Faculte de Medecine, Marseille, France.

European journal of clinical chemistry and clinical biochemistry - journal of the Forum of European Clinical Chemistry Societies (GERMANY) Sep 1996, 34 (9) p741-8, ISSN 0939-4974 Journal Code: 9105775

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The literature abounds with reports showing discrepancies in immunoassays of proteins and peptides. Whereas the isomorphism and polymorphism of proteins remains largely hidden in immunoassays making use of polyclonal antibodies, the use of **monoclonal** antibodies uncovered the difficulty of accurately assaying microheterogeneous analytes. Indeed, most proteic hormones are not entities with unique structures but rather mixtures of molecular forms with slight differences in structure which may reflect large variations in biological and immunological activities; the **monoclonal** antibodies appeared clearly less suited than the polyclonal for testing a mixture of isoforms. Protein microheterogeneity also has an impact on assay standardisation, since reference preparations may contain several isoforms of the analyte. Using recombinant glycoprotein does not solve the problem. Regarding the problem of discrepancy in immunoanalysis of proteins and peptides, we could establish, in a previous work, that discrepancy among lutropin assay kits may be related to various causes: i) differences in standard preparation and calibration curves; ii) microheterogeneity of lutropin molecules leading to missing some isoforms due to the restricted epitopic specificity of the **monoclonal** antibodies used in the kits. The epitopic dissection we engaged in appeared thus instrumental in explaining these discrepancies. It allowed us to enumerate epitopes on the surface of lutropin molecules, to elucidate the immunological structure and, finally, to characterize **monoclonal** antibodies used in commercially available lutropin assay kits with regard to their epitopic specificity. This work allowed us to interpret the discrepancy in serum lutropin concentration which was related to the use of **monoclonal** antibody with given specificity. Epitopic dissection may thus be instrumental in explaining discrepancy among immunoassays of proteins and peptides and in improving the accuracy of kits. (19 Refs.)

Tags: Female; Human; Male; Support, Non-U.S. Gov't

Descriptors: *Epitopes--chemistry--CH; *Immunoassay--methods--MT; *Peptides--chemistry--CH; *Proteins--chemistry--CH; Antibodies, **Monoclonal**; Kidney Failure--blood--BL; Luteinizing Hormone--blood--BL; **Menopause**--blood--BL; Polycystic Ovary Syndrome--blood--BL; Polymorphism (Genetics); Reagent Kits, Diagnostic--standards--ST; Reference Values

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Epitopes); 0 (Peptides); 0 (Proteins); 0 (Reagent Kits, Diagnostic); 9002-67-9 (Luteinizing Hormone)

Record Date Created: 19970206

Record Date Completed: 19970206

GalNAc is N-acetylgalactosamine and GlcNAc is N-acetylglucosamine). Ten percent of S-1 and of S-N had a bisecting GlcNAc residue. Sulphate residues occurred in nearly the same amount for both subunits; however, the alpha and beta subunits were sulphated differently. S-1 predominated in the alpha subunit, while S-1 and S-2 were major components in the beta subunit.(ABSTRACT TRUNCATED AT 250 WORDS)

Tags: Animal; Support, Non-U.S. Gov't

Descriptors: **Luteinizing Hormone** --chemistry--CH; *Oligosaccharides --chemistry--CH; Carbohydrate Conformation; Carbohydrate Sequence; Chromatography, Affinity; Chromatography, Ion Exchange; Electrochemistry; Methylation; Molecular Sequence Data; Molecular Structure; Oligosaccharides --isolation and purification--IP; Sulfates--chemistry--CH; Swine

CAS Registry No.: 0 (Oligosaccharides); 0 (Sulfates); 9002-67-9 (Luteinizing Hormone)

Record Date Created: 19920915

Record Date Completed: 19920915

14/9/22

DIALOG(R)File 155:MEDLINE(R)

07314234 92177208 PMID: 1795252

Comparison of the microheterogeneity of horse LH and FSH in the pituitary with that secreted into pituitary venous blood at oestrus.

Shand N; Alexander S L; Irvine C H

Department of Animal & Veterinary Sciences, Lincoln University, Canterbury, New Zealand.

Journal of reproduction and fertility. Supplement (ENGLAND) 1991, 44 p1-11, ISSN 0449-3087 Journal Code: 0225652

Contract/Grant No.: DK38322; DK; NIDDK

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

For aqueous extracts of pituitary glands of oestrous mares, luteinizing hormone (LH) profiles were found to be similar to each other and to earlier work after chromatofocussing (CF) and isoelectricfocussing (IEF). After CF, both LH and follicle-stimulating hormone (FSH) in pituitary extracts focussed in multiple peaks in the acidic range, with 86% of LH and 80% of FSH found between pH 4 and 6. By contrast, in pituitary venous plasma, only 18% of the LH focussed in this range, whereas a significantly greater proportion (P less than 0.01) eluted above pH 7 than occurred in pituitary extracts (37% vs 2%, respectively). For pituitary venous FSH, there was only a slight shift in the distribution of **isoforms** compared with the pituitary extract, with a rise in the percentage of strongly acidic molecules in pituitary venous plasma (pH less than 3.65; 34% vs 16%). These results show that at oestrus, horse LH (which differs from that of other species because it has a heavily **sialylated** C-terminal extension to the beta-subunit, as does eCG), is much more alkaline when secreted as opposed to when it is stored in the pituitary. The authors of this report suggest that this modification is made after entry into a preferentially released pool of LH. Modulation of the forms of LH and FSH that are secreted may play a role in regulating target tissue responses.

Tags: Animal; Comparative Study; Female; Support, U.S. Gov't, P.H.S.

Descriptors: Estrus--physiology--PH; * **Follicle Stimulating Hormone** --metabolism--ME; * **Gonadotropins** , Equine--metabolism--ME; *Horses --physiology--PH; * **Luteinizing Hormone** --metabolism--ME; *Pituitary Gland --physiology--PH; **Follicle Stimulating Hormone** --blood--BL; Isoelectric Point; **Luteinizing Hormone** --blood--BL

CAS Registry No.: 0 (Gonadotropins, Equine); 9002-67-9 (Luteinizing Hormone); 9002-68-0 (Follicle Stimulating Hormone)

Record Date Created: 19920407

Record Date Completed: 19920407

14/9/23

DIALOG(R)File 155:MEDLINE(R)

14/9/12
DIALOG(R)File 155:MEDLINE(R)
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10462449 96269272 PMID: 8778716
Isoforms **of luteinizing hormone]**
Izoformy hormonu luteinizujacego.
Szewczuk A; Kochanowska I E; Kurowska E
Laboratorium Biochemii Instytutu Immunologii i Terapii Doswiadczalnej PAN im. L. Hirszfelda we Wroclawiu.
Postepy higieny i medycyny doswiadczalnej (POLAND) 1996, 50 (1) p9-20, ISSN 0032-5449 Journal Code: 0421052
Document type: Journal Article; Review; Review, Tutorial ; English Abstract
Languages: POLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Luteinizing hormone (LH) is a heterodimeric glycoprotein containing varied amount of **sialic** acid. This is a reason of numerous LH **isoforms** called also isohormones. The hormone **isoforms** were separated usually by gel electrophoresis, isoelectrofocusing or chromatofocusing. They differ in biological and immunological activity. Human and some animals LH **isoforms** were reviewed. Also some genetic mutants of LH are described. Problems of the human **isoforms** for pathology and diagnostics are presented. (54 Refs.)
Tags: Animal; Female; Human
Descriptors: **Luteinizing Hormone** --physiology--PH; Adult; Child; Genital Diseases, Female--blood--BL; Genital Diseases, Female--diagnosis--DI; Kidney Diseases--diagnosis--DI; **Luteinizing Hormone** --analysis--AN; **Luteinizing Hormone** --chemistry--CH
CAS Registry No.: 9002-67-9 (Luteinizing Hormone)
Record Date Created: 19960917
Record Date Completed: 19960917

14/9/13
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

10352361 96155123 PMID: 8563483
Thyrotropic action of human chorionic gonadotropin .
Yoshimura M; Hershman J M
Second Department of Internal Medicine, Kansai Medical University, Osaka, Japan.
Thyroid - official journal of the American Thyroid Association (UNITED STATES) Oct 1995, 5 (5) p425-34, ISSN 1050-7256 Journal Code: 9104317
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Hyperthyroidism or increased thyroid function has been reported in many patients with trophoblastic tumors. In these cases, greatly increased human chorionic **gonadotropin** (hCG) levels and suppressed TSH levels suggest that hCG has thyrotropic activity. Recent investigations have clarified the structural homology not only in the hCG and TSH molecules but also in their receptors, and this homology suggests the basis for the reactivity of hCG with the TSH receptor. The clinical significance of the thyrotropic action of hCG is now also recognized in normal pregnancy and hyperemesis gravidarum. Highly purified hLH binds to recombinant hTSH receptor and is about 10 times as potent as purified hCG in increasing cAMP. The beta-subunits of hCG and hLH share 85% sequence identity in their first 114 amino acids but differ in the carboxy-terminal peptide because hCG beta contains a 31-amino acid extension (beta-CTP). A recombinant mutant hCG that lacks beta-CTP showed almost identical potency to LH on stimulation of recombinant hTSH receptor. If intact hCG were as potent as hLH in regard to

its thyrotropic activity, most pregnant women would become thyrotoxic. One of the roles of the beta-CTP may be to prevent overt hyperthyroidism in the first trimester of pregnancy when a large amount of hCG is produced by the placenta. Nicked hCG preparations, obtained from patients with trophoblastic disease or by enzymatic digestion of intact hCG, showed approximately 1.5- to 2-fold stimulation of recombinant hTSH receptor compared with intact hCG. This suggests that the thyrotropic activity of hCG may be influenced by the metabolism of the hCG molecule itself. Deglycosylation and/or desialylation of hCG enhances its thyrotropic potency. Basic hCG **isoforms** with lower **sialic** acid content extracted from hydatidiform moles were more potent in activating adenylate cyclase, and showed high bioactivity/immunoactivity (B/I) ratio in CHO cells expressing human TSH receptors. This is consistent with the finding that the beta-CTP truncated hCG with higher thyrotropic potency is substantially deglycosylated and desialylated in the beta-subunit relative to intact hCG because all four O-linked glycosylation sites occur within the missing C-terminal extension. The desialylated hCG variant also interacts directly with recombinant hTSH receptors transfected into human thyroid cancer cells. There is thyroid-stimulating activity in sera of normal pregnant women, and this correlates with serum hCG levels. The thyroid gland of normal pregnant women may be stimulated by hCG to secrete slightly excessive quantities of T4 and induce a slight suppression of TSH, perhaps being about 1 mU/L less than nongravid levels, but not high enough to induce overt hyperthyroidism. Maternal thyroid glands may secrete more thyroid hormone during early pregnancy in response to the thyrotropic activity of hCG that overrides the normal operation of the hypothalamic-pituitary-thyroid feedback system. Biochemical hyperthyroidism associated with hyperemesis gravidarum has been attributed to hCG. In patients with hyperemesis gravidarum, thyrotropic in serum correlated with hCG immunoreactivity, and the severity of vomiting as indicated by clinical and biochemical parameters correlated with the degree of thyroid stimulation. To understand the thyrotropic action of hCG, it is necessary to know whether hCG activates the same domain of the TSH receptor as does TSH. The identification of the molecular structure of the hCG **isoform** with the highest thyrotropic potency will resolve the enigma of gestational thyrotoxicosis and the hyperthyroidism associated with trophoblastic disease and hCG-producing tumors. (62 Refs.)

Tags: Animal; Female; Human; Pregnancy; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.

Descriptors: Chorionic **Gonadotropin** --pharmacology--PD; *Thyrotropin --pharmacology--PD; Amino Acid Sequence; Chorionic **Gonadotropin** --chemistry--CH; Molecular Sequence Data; Receptors, Thyrotropin--drug effects--DE; Sequence Homology; Thyrotropin--chemistry--CH

CAS Registry No.: 0 (Chorionic Gonadotropin); 0 (Receptors, Thyrotropin); 9002-71-5 (Thyrotropin)

Record Date Created: 19960301

Record Date Completed: 19960301

14/9/14

DIALOG(R)File 155:MEDLINE(R)

10339634 96141991 PMID: 8550754

More basic isoforms **of serum** gonadotropins **during** gonadotropin **-releasing hormone agonist therapy in pubertal children.**

Wide L; Albertsson-Wikland K; Phillips D J

Department of Clinical Chemistry, University Hospital, Uppsala, Sweden.

Journal of clinical endocrinology and metabolism (UNITED STATES) Jan 1996, 81 (1) p216-21, ISSN 0021-972X Journal Code: 0375362

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

An acute challenge of exogenous GnRH elicits rapidly increased serum **gonadotropin** levels with qualitative changes to more basic **isoforms** of both FSH and LH. Chronic GnRH agonist therapy suppresses endogenous **gonadotropins** , and the serum levels of FSH and LH are low and fairly

constant. A possible qualitative change in the **gonadotropins** during GnRH agonist therapy was investigated by determination of the median charge of the **gonadotropin isoforms** before and during therapy in 18 pubertal children. Two different GnRH agonists were studied: buserelin, given intranasally or as a sc implant for 1.5-34 months to five girls, aged 7-10 yr, and for 5-6 months to two boys, aged 11-13 yr; and triptorelin, administered as a depot preparation for 3-6 months to four girls, aged 9-12.5 yr, and for 1-24 months to seven boys, aged 10.5-12 yr. FSH and LH in serum and eluates after electrophoresis in 0.10% agarose suspension were measured with sandwich fluoroimmunoassays. The mean serum FSH and LH levels decreased significantly ($P < 0.05$) in girls during triptorelin therapy, whereas only the FSH level decreased ($P < 0.05$) in the boys. There were no significant ($P > 0.05$) changes in serum **gonadotropin** levels during buserelin therapy. All of the children had more basic serum **isoforms** of LH, and all but one had more basic forms of FSH during the GnRH agonist treatments. In a girl who had more basic **gonadotropin isoforms** after treatment with triptorelin for 2 and 6 months, a GnRH challenge elicited the release of still more basic **isoforms** . The changes in mean median charge to more basic **gonadotropin isoforms** were highly significant for both busereline ($P < 0.01$) and triptorelin ($P < 0.001$) treatment. An increased ($P < 0.001$) degree of charge heterogeneity was observed for FSH after triptorelin therapy. These findings show that there is a qualitative change in the **isoforms** of both FSH and LH in serum during GnRH agonist therapy in pubertal children. The changes in charge to more basic **gonadotropin isoforms** most likely reflect a direct effect at the pituitary level, leading to the synthesis and/or selective release of less **sialylated** and sulfated **isoforms** of the **gonadotropins** . The observed qualitative changes in the **gonadotropin isoforms** in these pubertal children may be part of the clinical effects of GnRH-agonist-therapy, leading to an arrest or regression of puberty.

Tags: Female; Human; Male

Descriptors: Buserelin--therapeutic use--TU; * **Follicle Stimulating Hormone** --blood--BL; * **Luteinizing Hormone** --blood--BL; *Puberty--blood--BL ; *Triptorelin--therapeutic use--TU; Adolescent; Child

CAS Registry No.: 57773-63-4 (Triptorelin); 57982-77-1 (Buserelin); 9002-67-9 (Luteinizing Hormone); 9002-68-0 (Follicle Stimulating Hormone)

Record Date Created: 19960220

Record Date Completed: 19960220

14/9/15

DIALOG(R)File 155:MEDLINE(R)

08644045 95332639 PMID: 7608469

Application of a sensitive HPLC-based fluorometric assay to determine the sialic **acid content of human** gonadotropin isoforms .

Stanton P G; Shen Z; Kecorius E A; Burgon P G; Robertson D M; Hearn M T

Centre for Bioprocess Technology, Monash University, Victoria, Australia.

Journal of biochemical and biophysical methods (NETHERLANDS) Feb 1995, 30 (1) p37-48, ISSN 0165-022X Journal Code: 7907378

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The human pituitary **gonadotropins** , follitropin (hFSH) and lutropin (hLH) are glycoproteins which are microheterogeneous in terms of their charge and molecular size, as well as their in vitro and in vivo bioactivities. The aim of this study was to determine the contribution of variations in **sialic** acid (N-acetyl neuraminic acid) content to the structural heterogeneity of these glycoproteins. **Sialic** acid (Neu5Ac) was released by partial acid hydrolysis (0.1 M TFA, 80 degrees C, 1 h) and derivatised with the fluorescent label DMB (1,2-diamino-4,5-methylenedioxyb enzene) in conjunction with an internal standard (N-glycoyl-neuraminic acid). The derivatives were then separated by reversed-phase HPLC. This method allowed quantitation of the **sialic** acid content over a range of 5-100 pmol with between assay variation of < 6% for **sialic** acid released

from approximately 100 ng (3 pmol) of hFSH or hLH. Comparison of the **sialic** acid contents of standard **sialylated** glycoproteins by either DMB-derivatisation or high-performance anion-exchange chromatography with pulsed amperometric detection yielded similar results, confirming the reliability of the fluorescence detection method. The **sialic** acid contents of 9 hFSH **isoforms** varied between 1.5-13.7 mol Neu5AC/mol FSH, whilst a range of 1.1-9.1 mol Neu5AC/mol LH was observed for 12 hLH **isoforms**. The **sialic** acid content of the hFSH **isoforms** was also observed to be related to the hormonal specific activity in a radioreceptor assay, confirming that alterations in the carbohydrate structure can influence the FSH-receptor interaction. In contrast, the **sialic** acid content of the hLH **isoforms** was found to be not related to specific activity at the receptor level.

Tags: Human; Support, Non-U.S. Gov't

Descriptors: Chromatography, High Pressure Liquid; *Fluorometry--methods --MT; * **Follicle Stimulating Hormone** --chemistry--CH; * **Luteinizing Hormone** --chemistry--CH; * **Sialic** Acids--analysis--AN; Fluorescent Dyes; Hydrolysis; Linear Models; N-Acetylneuraminic Acid; Phenylenediamines; Reference Standards; Sensitivity and Specificity

CAS Registry No.: 0 (Fluorescent Dyes); 0 (Phenylenediamines); 0 (Sialic Acids); 131-48-6 (N-Acetylneuraminic Acid); 38608-07-0 (1,2-diamino-4,5-methylenedioxybenzene); 9002-67-9 (Luteinizing Hormone); 9002-68-0 (Follicle Stimulating Hormone)

Record Date Created: 19950817

Record Date Completed: 19950817

14/9/16

DIALOG(R)File 155:MEDLINE(R)

08575420 95263722 PMID: 7745007

Variation in the thyrotropic activity of human chorionic gonadotropin **in Chinese hamster ovary cells arises from differential expression of the human thyrotropin receptor and microheterogeneity of the hormone.**

Hoermann R; Poertl S; Liss I; Amir S M; Mann K

Department of Medicine, University of Essen, Germany.

Journal of clinical endocrinology and metabolism (UNITED STATES) May 1995, 80 (5) p1605-10, ISSN 0021-972X Journal Code: 0375362

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

The role of hCG as a stimulator of the human thyroid has been a subject of controversy, because discrepant results have been obtained in different in vitro assays. In an attempt to explain the variation observed in the thyroid response to hCG, we investigated the ability of hCG and that of its **isoforms** and glycosylation variants to inhibit [125I]bovine (b) TSH binding and stimulate adenylate cyclase in two clones, JP09 and JP26, of Chinese hamster ovary cells stably transfected with the human TSH receptor (hTSHr). The two clones differed with respect to the number of hTSHr expressed per cell (34,000 in JP09 and 2,000 in JP26 cells). Both responded extremely well to bTSH; the cAMP response to 0.001 IU/L bTSH was distinguishable from basal values. Interestingly, JP09 cells were readily stimulated by hCG (20-100 mg/L; 0.52-2.6 x 10(-6) mol/L) to release cAMP, whereas JP26 cells showed little if any response. Also, cAMP stimulation produced by asialo-hCG was 12-fold in JP09 cells and only 4-fold in JP26 cells compared to 45- and 67-fold stimulations by bTSH, respectively. Stimulation by asialo-hCG was approximately 30% that of bTSH in JP09 cells, but less than 6% in JP26 cells. When assessing the thyrotropic activity of the microheterogeneous **isoforms** of hCG, more alkaline pI forms were found to be more active than those of a more acidic pI regardless of whether they were derived from normal or molar pregnancy urine. Further studies with hCG, asialo-hCG, asialoagalacto-hCG, and deglycosylated hCG revealed that removal of **sialic** acid caused a marked increase in both its affinity for hTSHr and its cAMP-releasing potency, whereas removal of further carbohydrate, although it slightly enhanced receptor binding, was detrimental to adenylate cyclase activation. In conclusion, differences in

hTSHr expression may cause a variation in the cAMP response to hCG or its glycosylation variants, as does the microheterogeneity of the hormone itself. These mechanisms may be responsible at least in part for the divergent responses of different cell types to hCG and render interpretation of the physiological meaning of the data obtained in recombinant receptor systems difficult.
Tags: Animal; Human; Support, Non-U.S. Gov't
Descriptors: CHO Cells--metabolism--ME; *Chorionic **Gonadotropin** --pharmacology--PD; *Receptors, Thyrotropin--metabolism--ME; *Thyrotropin --metabolism--ME; Asialoglycoproteins--pharmacology--PD; Chorionic **Gonadotropin** --chemistry--CH; Cyclic AMP--metabolism--ME; Hamsters; Infant, Newborn; Isomerism; Thyrotropin--antagonists and inhibitors--AI
CAS Registry No.: 0 (Asialoglycoproteins); 0 (Chorionic Gonadotropin); 0 (Receptors, Thyrotropin); 0 (asialo-human chorionic gonadotropin); 60-92-4 (Cyclic AMP); 9002-71-5 (Thyrotropin)
Record Date Created: 19950615
Record Date Completed: 19950615

14/9/17
DIALOG(R)File 155:MEDLINE(R)

08512464 95200740 PMID: 7765934
Role of environmental conditions on the expression levels, glycoform pattern and levels of sialyltransferase **for hFSH produced by recombinant CHO cells.**
Chotigeat W; Watanapokasin Y; Mahler S; Gray P P
Department of Biotechnology, University of New South Wales, Sydney, Australia.
Cytotechnology (NETHERLANDS) 1994, 15 (1-3) p217-21, ISSN 0920-9069
Journal Code: 8807027
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: BIOTECHNOLOGY
A recombinant CHO cell line in which the expression of human follicle stimulating hormone (hFSH) was under the control of the beta actin promoter was maintained in steady state perfusion cultures on a protein free medium. The level of expression of the hFSH was controlled by varying the steady state level of dissolved oxygen (10-90% of air saturation) and of sodium butyrate (0-1.5mM). Under these conditions, the specific productivity of hFSH (qFSH) varied from 0.7 to 4.8 ng hFSH/10(6) cells/h. As the specific productivity of hFSH increased, there was a shift in the FSH **isoforms** to the lower pI fractions, corresponding to increased **sialic** acid content. As the specific productivity of hFSH increased, shifting the **isoform** distribution towards the lower pI **isoforms** , that the **sialyltransferase** enzymic activity also increased.
Tags: Animal; Human; Support, Non-U.S. Gov't
Descriptors: **Follicle Stimulating Hormone** --biosynthesis--BI; *Recombinant Proteins--biosynthesis--BI; * **Sialyltransferases** --metabolism --ME; *Tissue Culture--methods--MT; Actins--genetics--GE; Biotechnology --instrumentation--IS; Biotechnology--methods--MT; Butyric Acid; Butyric Acids--pharmacology--PD; CHO Cells; Gene Expression; Glycosylation; Hamsters; Kinetics; Oxygen--pharmacology--PD; Promoter Regions (Genetics); **Sialic** Acids--metabolism--ME; Time Factors
CAS Registry No.: 0 (Actins); 0 (Butyric Acids); 0 (Recombinant Proteins); 0 (Sialic Acids); 107-92-6 (Butyric Acid); 7782-44-7 (Oxygen); 9002-68-0 (Follicle Stimulating Hormone)
Enzyme No.: EC 2.4.99.- (**Sialyltransferases**)
Record Date Created: 19950425
Record Date Completed: 19950425

14/9/18
DIALOG(R)File 155:MEDLINE(R)

08291837 94358076 PMID: 8077357

Increased biological activity due to basic isoforms in recombinant human follicle-stimulating hormone produced in a human cell line.

Flack M R; Bennet A P; Froehlich J; Anasti J N; Nisula B C

Developmental Endocrinology Branch, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland 20892.

Journal of clinical endocrinology and metabolism (UNITED STATES) Sep 1994, 79 (3) p756-60, ISSN 0021-972X Journal Code: 0375362

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

FSH has four asparagine-linked oligosaccharides with variable **sialic** acid contents, so that FSH is not a single molecule, but a heterogeneous group of **isoforms** . These **isoforms** differ in their biological properties and their distribution changes in various physiological states, allowing the modulation of FSH activity. Recombinant human (h) FSH has been produced in Chinese hamster ovary cells and has an **isoform** profile similar to those of both pituitary FSH standard and purified urinary FSH. These FSH preparations, however, do not contain the full spectrum of FSH **isoforms** found in the circulation. Production of recombinant hFSH in a cell line with a different pattern of glycosylation could broaden its **isoform** profile and potentially alter its biological activity. Thus, we transfected human embryonal kidney cells (293) with the human alpha and FSH beta genes to produce recombinant hFSH (hFSH-293) and determined its biological activity in a rat granulosa cell bioassay. Although hFSH-293 was immunologically indistinguishable from pituitary FSH standard, its biological potency was 3- to 6-fold higher than those of two different pituitary FSH standards. To investigate this increased potency, we separated the **isoforms** of hFSH-293 by chromatofocusing and determined their biological potencies in the rat granulosa cell bioassay. The **isoform** profile of hFSH-293 demonstrated a greater number of basic **isoforms** than that of pituitary FSH standard. Several of these basic **isoforms** exhibited enhanced in vitro biological potency, accounting for the increased biological potency of hFSH-293. This pattern of high in vitro biological activity and more basic **isoforms** is analogous to the FSH circulating during GnRH stimulation, pubertal induction, and ovulation.

Tags: Animal; Female; Human

Descriptors: **Follicle Stimulating Hormone** --chemistry--CH; * **Follicle Stimulating Hormone** --pharmacology--PD; Cell Line; Chromatography; Embryo; Estradiol--biosynthesis--BI; **Follicle Stimulating Hormone** --genetics--GE; Glycosylation; Granulosa Cells--drug effects--DE; Granulosa Cells --metabolism--ME; Hydrogen-Ion Concentration; Immunoassay; Kidney; Rats; Recombinant Proteins--metabolism--ME; Transfection

CAS Registry No.: 0 (Recombinant Proteins); 50-28-2 (Estradiol); 9002-68-0 (Follicle Stimulating Hormone)

Record Date Created: 19941006

Record Date Completed: 19941006

14/9/19

DIALOG(R)File 155:MEDLINE(R)

08143503 94209372 PMID: 8157712

Thyrotropic activity of basic isoelectric forms of human chorionic gonadotropin extracted from hydatidiform mole tissues.

Yoshimura M; Pekary A E; Pang X P; Berg L; Goodwin T M; Hershman J M

Endocrinology Research Laboratory, West Los Angeles Veterans Affairs Medical Center, California 90073.

Journal of clinical endocrinology and metabolism (UNITED STATES) Apr 1994, 78 (4) p862-6, ISSN 0021-972X Journal Code: 0375362

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

hCG is known to have thyroid-stimulating activity and may cause hyperthyroidism in patients with trophoblastic diseases. hCG occurs in normal and molar pregnancy with breaks or nicks in the alpha- or beta-subunit peptide linkage and with substantial heterogeneity in the composition and degree of branching within the oligosaccharide side-chains. The bioactivity of hCG is markedly influenced by these structural variations. We purified hCG from five hydatidiform moles, using chromatofocusing separation after gel filtration. The hCG molecules were fractionated according to their isoelectric points, with a linear pH gradient from 3.2-6.1 and a final 1.0 mol/L NaCl step elution. The hCG immunoreactivity of each fraction was measured by RIA, and the thyroid-stimulating activity of hCG was determined by means of the cAMP response in Chinese hamster ovary cells expressing functional human TSH receptors (Chinese hamster ovary-JP09 cells). The chromatofocusing profile showed that hCG from the moles was eluted in six or seven major peaks at pH 6.1, 5.5, 5.3, 4.8, 3.8, and 3.2 and with 1.0 mol/L NaCl, whereas hCG extracted from serum of hydatidiform moles and standard hCG preparation CR-127 extracted from pregnancy urine showed only small peaks at pH greater than 5.3. Each fraction increased cAMP production significantly in Chinese hamster ovary-JP09 cells. The relative bioactivity/immunoreactivity, represented as the ratio of cAMP/hCG (picomoles per IU), was significantly higher in basic components (pI 6.1, 6.2 +/- 1.2; pI 5.5, 4.4 +/- 2.7; pI 5.3, 5.8 +/- 0.3) than in hCG CR-127 (bioactivity/immunoreactivity, 0.42; P < 0.05). The difference in pI of each hCG **isoform** was attributable to the extent of **sialylation** ; basic hCG **isoforms** contained less **sialic** acid by immunological detection using lectins. These results indicate that **isoforms** of hCG with more thyrotropic activity were produced by trophoblastic tissues in patients with hydatidiform mole. We speculate that these **isoforms** of hCG may be responsible for the hyperthyroidism in some patients with hydatidiform moles.

Tags: Animal; Female; Human; Pregnancy; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.

Descriptors: Chorionic **Gonadotropin** --analysis--AN; *Chorionic **Gonadotropin** --physiology--PH; *Hydatidiform Mole--chemistry--CH; *Thyroid Gland--physiology--PH; *Uterine Neoplasms--chemistry--CH; Adult; CHO Cells; Chorionic **Gonadotropin** --blood--BL; Cyclic AMP--metabolism--ME; Hamsters; Hydatidiform Mole--pathology--PA; Hydrogen-Ion Concentration; Isoelectric Focusing; Isomerism; Radioimmunoassay; Receptors, Thyrotropin--analysis--AN ; Receptors, Thyrotropin--physiology--PH; Thyroid Gland--chemistry--CH; Thyroid Gland--ultrastructure--UL; Uterine Neoplasms--pathology--PA

CAS Registry No.: 0 (Chorionic Gonadotropin); 0 (Receptors, Thyrotropin); 60-92-4 (Cyclic AMP)

Record Date Created: 19940519

Record Date Completed: 19940519

14/9/20

DIALOG(R)File 155:MEDLINE(R)

07736119 93191397 PMID: 1294011

[Glycoprotein hormones, glycosylation and biological activity]

Hormones glycoproteiques, glycosylation et activite biologique.

Pigny P; Berault A; Dewailly D; Boersma A

Laboratoire d'endocrinologie, USN A, CHU Lille, France.

Annales de biologie clinique (FRANCE) 1992, 50 (8) p557-64, ISSN 0003-3898 Journal Code: 2984690R

Document type: Journal Article; Review; Review, Tutorial ; English Abstract

Languages: FRENCH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Glycoprotein hormones LH, FSH, TSH and hCG are heterodimeric molecules: each contains two subunits, a common alpha and a unique beta subunit. Each subunit bears one or two Asparagine linked carbohydrate moieties which have a biantennary complex-type or hybrid-type structure. Different technical methods as deglycosylation or molecular biology techniques have been used to study the role of carbohydrate residues in hormonal bioactivity. The

carbohydrate chains are not directly involved in receptor binding events but their mechanisms of action is not fully understood. Two hypotheses are frequently emphasised: a conformational role or an involvement in the coupling of the receptor-adenylate cyclase system. At the post receptor level carbohydrate chains modulate the bioactivity in two ways: a global regulation following an all-or-none mode and slight one. The removal of the carbohydrate moieties leads to a loss of the in vitro hormonal activity. The results observed are dependent of the deglycosylation techniques and the bioactivity tests used. Hormone's deglycosylation reduces their capacity of production of cAMP and, to a lesser extent, their steroidogenic power. Deglycosylated hormones are antagonists to negative hormones although deglycosylated hCG has some agonist properties in vivo. Microheterogeneity of the glycoprotein hormones is due to slight variations in **sialic** acid and/or sulfate content. Glycoprotein hormones exist as several **isoforms** which differ in biological potency. Alkaline **isoforms** (less **sialylated** ones) are the most biologically active in vitro but have a short half live in vivo; acid **isoforms** are less active in vitro but have a longer circulatory half live. The polymorphism of glycoprotein hormones is a highly regulated process.(ABSTRACT TRUNCATED AT 250 WORDS) (74 Refs.)

Tags: In Vitro

Descriptors: Chorionic **Gonadotropin** --metabolism--ME; * **Follicle Stimulating Hormone** --metabolism--ME; * **Luteinizing Hormone** --metabolism --ME; *Thyrotropin--metabolism--ME; Glycosylation; Polysaccharides --metabolism--ME; Receptors, FSH--metabolism--ME; **Receptors, Gonadotropin --metabolism** --ME; Receptors, LH--metabolism--ME; Receptors, Thyrotropin --metabolism--ME

CAS Registry No.: 0 (Chorionic Gonadotropin); 0 (Polysaccharides); 0 (Receptors, FSH); 0 (Receptors, Gonadotropin); 0 (Receptors, LH); 0 (Receptors, Thyrotropin); 9002-67-9 (Luteinizing Hormone); 9002-68-0 (Follicle Stimulating Hormone); 9002-71-5 (Thyrotropin)

Record Date Created: 19930407

Record Date Completed: 19930407

14/9/21

DIALOG(R)File 155:MEDLINE(R)

07497280 92360983 PMID: 1498420

Subunit-specific sulphation of oligosaccharides relating to charge-heterogeneity in porcine lutrophin isoforms .

Ujihara M; Yamamoto K; Nomura K; Toyoshima S; Demura H; Nakamura Y; Ohmura K; Osawa T

Department of Medicine, Tokyo Women's Medical College, Japan.

Glycobiology (ENGLAND) Jun 1992, 2 (3) p225-31, ISSN 0959-6658 Journal Code: 9104124

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

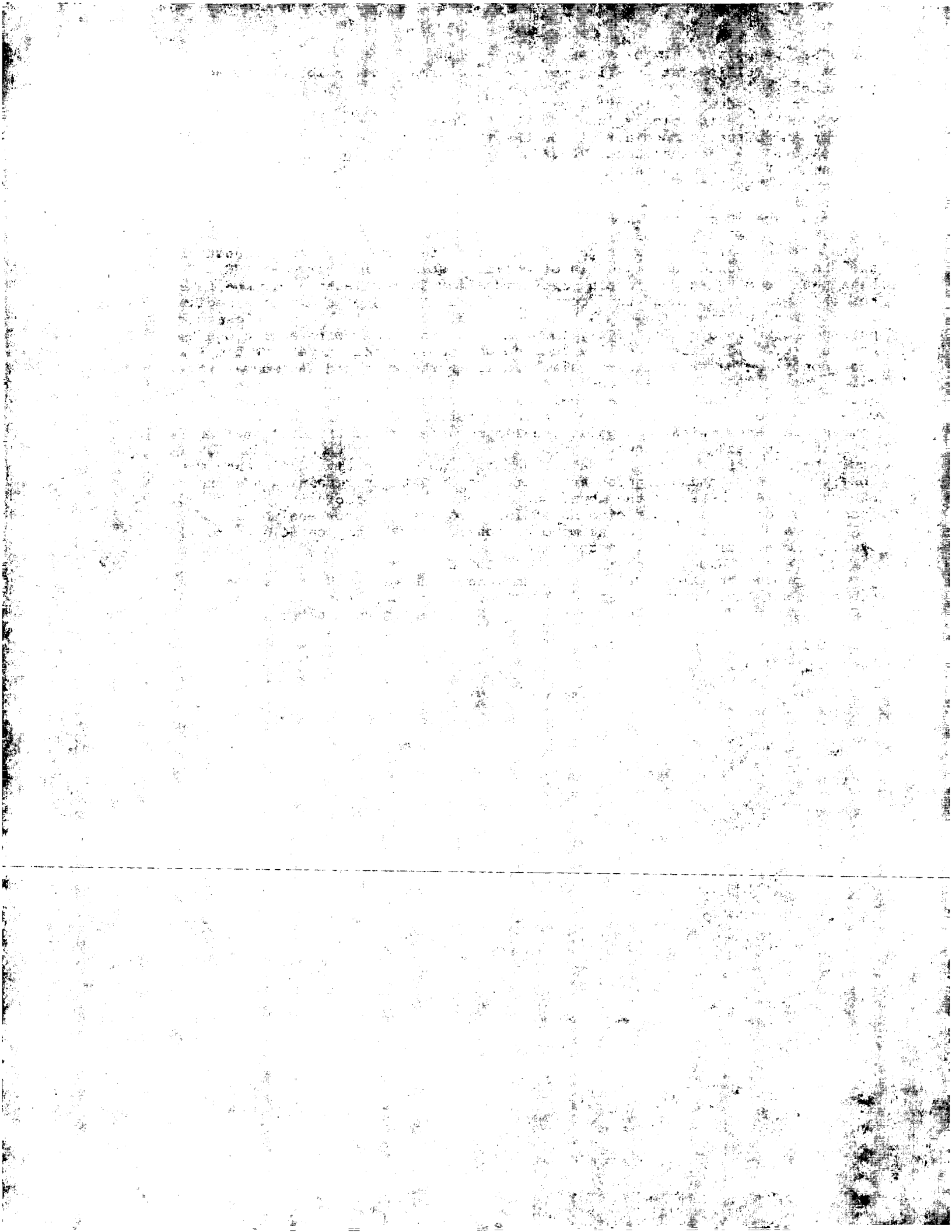
Subfile: INDEX MEDICUS

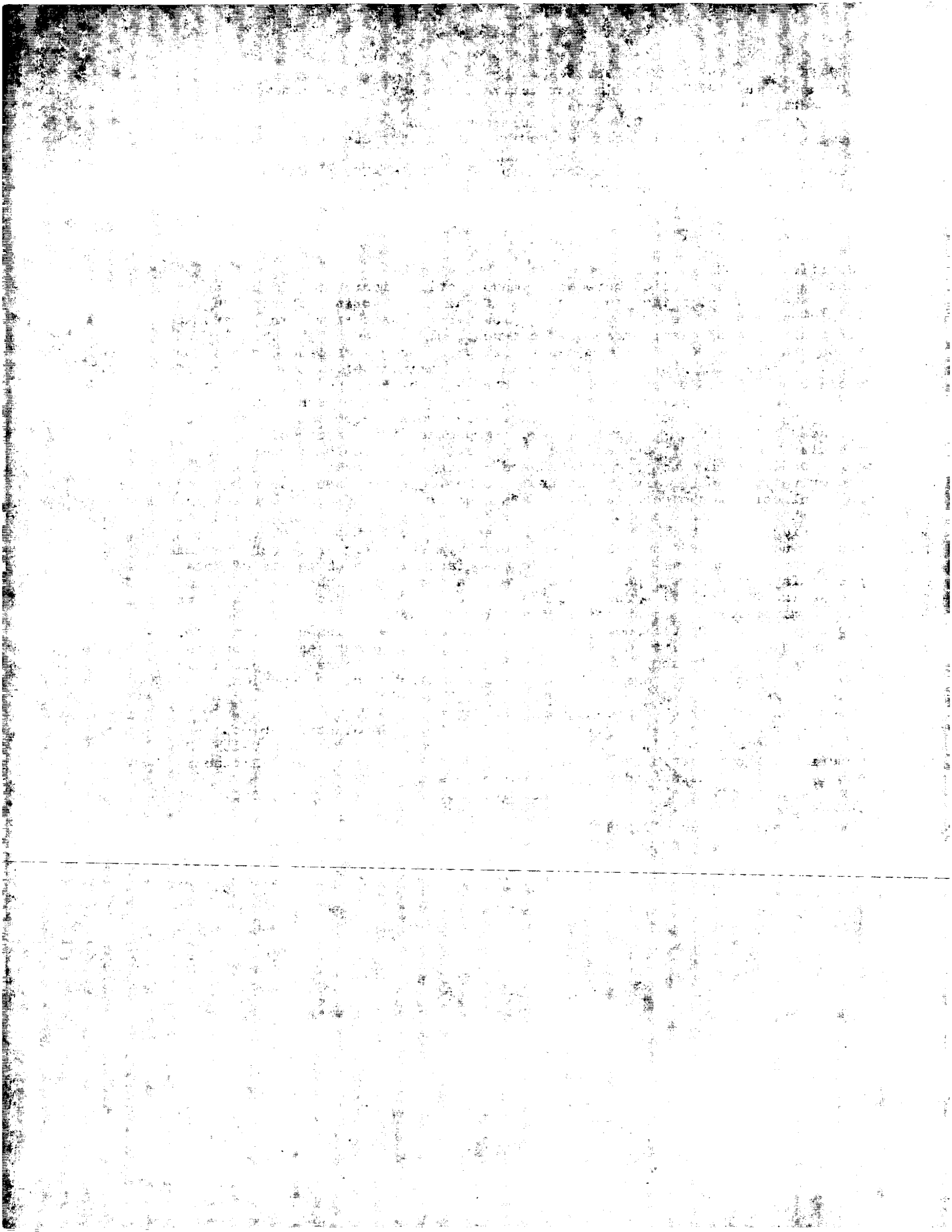
Lutrophin (LH) consists of an array of **isoforms** with different charges and bioactivities. This study was undertaken to clarify specifically how oligosaccharides of alpha and beta subunits contribute to LH **isoform** charges. Porcine LH (pLH) was separated into four **isoforms** by isoelectric focusing (IEF), followed by subunit isolation. Their oligosaccharides were released by hydrazinolysis, labelled by reduction with NaB3H4, and fractionated by HPLC with a Mono Q column into five populations differing in the number of sulphate (S) and **sialic** acid (N) residues, designated as Neutral, N-1, S-1, S-N and S-2. Oligosaccharides were predominantly sulphated (S-1 and S-2) and infrequently **sialylated** (N-1 and S-N). Further analysis, including concanavalin A (Con A) affinity chromatography, desialylation, desulphation, sequential exoglycosidase digestion and methylation, clarified the structures of the acidic oligosaccharides. All were of the biantennary complex type. Their two peripheral branches were SO4-4GalNAc beta 1-4Glc-NAc and GalNAc beta 1-4GlcNAc or GlcNAc in S-1, SO4-4GalNAc beta 1-4GlcNAc and Sia alpha 2-6Gal beta 1-4GlcNAc in S-N, and (SO4-4GalNAc beta 1-4GlcNAc)2 in S-2 (where

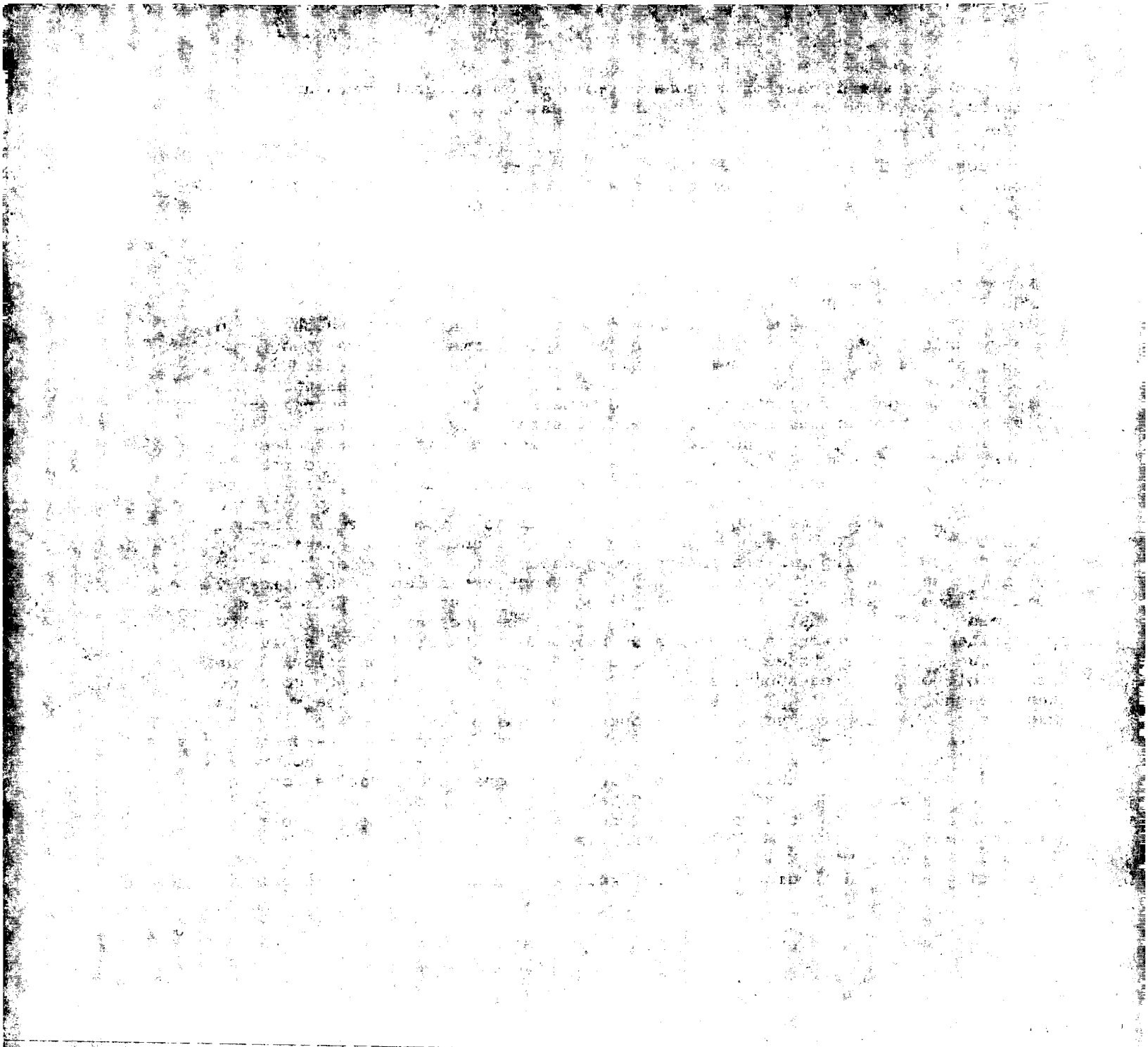
CAS Registry No.: 0 (Chorionic Gonadotropin); 0 (Glycoproteins); 0 (Pituitary Hormones); 0 (Recombinant Proteins); 9002-67-9 (Luteinizing Hormone); 9002-68-0 (Follicle Stimulating Hormone); 9002-71-5 (Thyrotropin)
Record Date Created: 19970206
Record Date Completed: 19970206

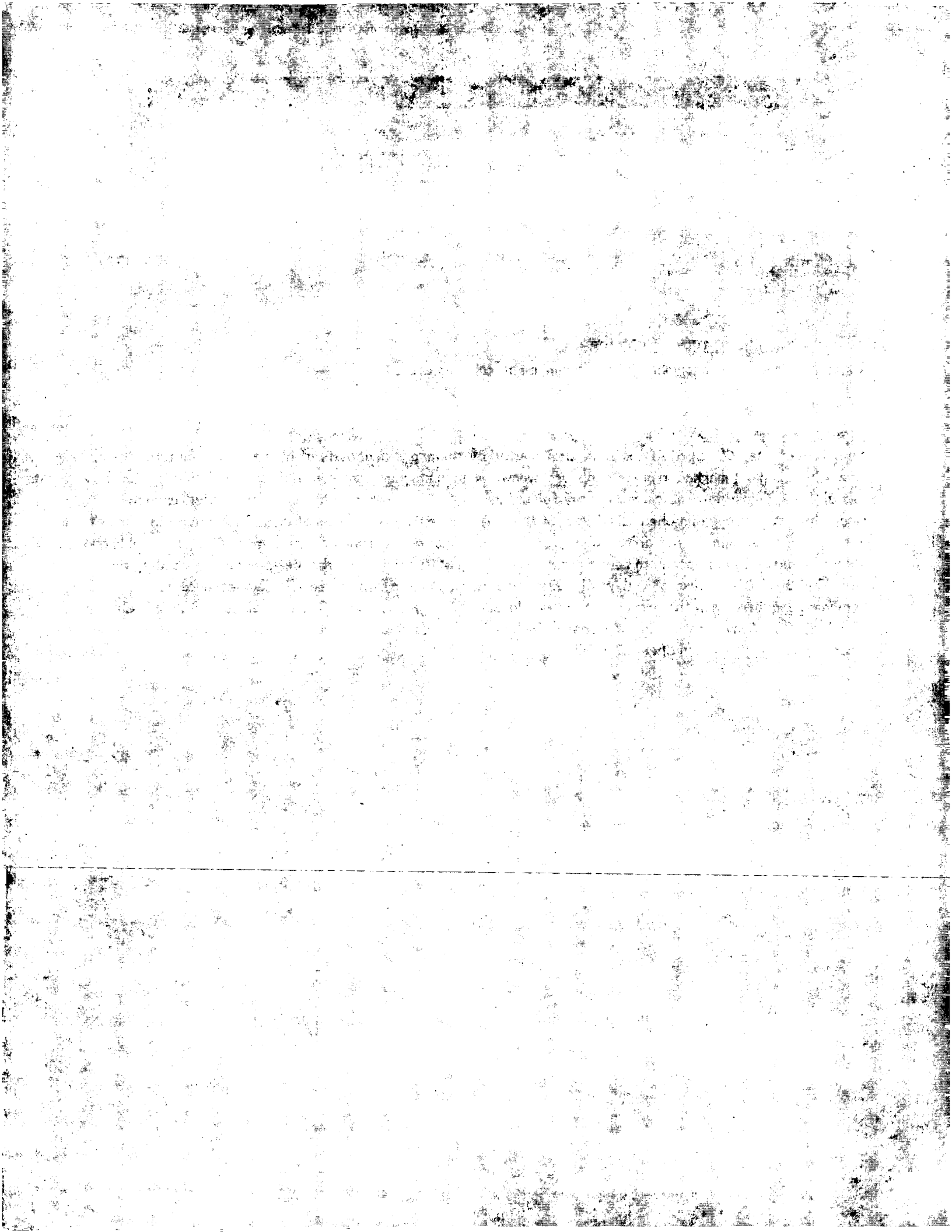
14/9/11
DIALOG(R)File 155:MEDLINE(R)

10682748 97031915 PMID: 8877821
Molecular heterogeneity and glycosylation modulation of rat pituitary prolactin isoforms synthesized and secreted in vitro in postnatal ontogeny, gestation, lactation and weaning.
Bollengier F; Mahler A; Matton A; Vanhaelst L
Laboratorium voor Farmacologie, Faculteit Geneeskunde en Farmacie, Vrije Universiteit Brussel, Belgium.
Journal of neuroendocrinology (ENGLAND) Sep 1996, 8 (9) p721-30, ISSN 0953-8194 Journal Code: 8913461
Erratum in J Neuroendocrinol 1996 Dec;8(12) 908
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
The modulation of both the molecular size heterogeneity and the relative distribution of rat **prolactin** variants, synthesized and secreted in vitro by rat pituitary cells in the course of postnatal ontogeny and in gestation, lactation and weaning was investigated by SDS-PAGE, immunoblotting, radioimmunological techniques and O- **sialoendopeptidase** digestion. The outcome of the experiments is as follows: 1) from day 1 of postnatal life 20-, 23-, 26-, 40-44 kDa and oligomeric rat **prolactin** **isoforms** were stored and secreted; 2) perinatal life is characterized by a high degree of variability of **prolactin** size **isoforms** and their respective repartition in storage and release; in addition to the major variants, transient ones of M, 25-, 28-, 33- and 36 kDa were secreted and/or stored; 3) O- **sialoglycoprotease** digestion of pituitary cell lysate gave good evidence for 25 kDa **prolactin** being a glycoform; 4) at 1 month of age 16 kDa rat **prolactin** appeared and persisted over the whole postnatal span (1 day-->1 year) but only in stored form; 5) the physiology of gestation was essentially characterized by the M(r)-modulation of the glycoform (26 kDa-->26.3 kDa) and the virtual absence of stored 26 kDa rat **prolactin** at week 1 of pregnancy; 6) in lactation and weaning uncommon multiple banding was observed in secreted oligomeric **prolactin** ; 7) in pregnancy, lactation and weaning the differential distribution of released and stored **prolactin** **isoforms** displayed a considerable intra- and intervariability; 8) in the vast array of size **isoforms** observed in all our experiments monomeric 23 kDa **prolactin** was always the dominating variant. In conclusion, the molecular size heterogeneity and the differential distribution of secreted and stored rat pituitary **prolactin** is considerably influenced by age and physiological stimuli. The nature of polymeric **prolactin** and of the transient variants is presently unclear, and the exact physiological role of molecular heterogeneity modulation is unknown, both in humans and rat, but the patterns of change we observed in definite stages of life, suggest that this phenomenon is important in the maturation of the hypothalamus-pituitary axis and in the metabolic and hormonal changes accompanying gestation.
Tags: Animal; Female; Pregnancy; Support, Non-U.S. Gov't
Descriptors: Pituitary Gland--physiology--PH; * **Prolactin** --metabolism --ME; Glycosylation; Isomerism; Lactation--physiology--PH; Pituitary Gland --embryology--EM; Pituitary Gland--growth and development--GD; **Prolactin** --biosynthesis--BI; **Prolactin** --secretion--SE; Rats; Rats, Wistar; Weaning
CAS Registry No.: 9002-62-4 (Prolactin)
Record Date Created: 19970110
Record Date Completed: 19970110









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ormation:
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?b 155

       04jun03 16:21:13 User228206 Session D1981.1
            $0.00    0.159 DialUnits FileHomeBase
     $0.00  Estimated cost FileHomeBase
     $0.00  Estimated cost this search
     $0.00  Estimated total session cost   0.159 DialUnits


File 155:MEDLINE(R)  1966-2003/Jun W1
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*File 155: Medline has been reloaded and accession numbers have
changed.  Please see HELP NEWS 155.

      Set  Items  Description
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?e gonadotropin

Ref    Items  Index-term
E1         2  GONADOTROPIINIRESEPTORIT
E2         1  GONADOTROPIINIT
E3     37744 *GONADOTROPIN
E4     20838  GONADOTROPIN //CHORIONIC (CHORIONIC GONADOTROPIN)
E5       223  GONADOTROPIN //RECEPTORS, (RECEPTORS, GONADOTROPIN)
E6         2  GONADOTROPIN I BETA SUBUNIT, FUNDULUS
E7         5  GONADOTROPIN I BETA-SUBUNIT, BASS
E8         2  GONADOTROPIN I, KATSUWONUS
E9         1  GONADOTROPIN I, TUNA
E10        2  GONADOTROPIN II ALPHA SUBUNIT, CATFISH
E11        4  GONADOTROPIN II BETA SUBUNIT, BASS
E12        5  GONADOTROPIN II BETA SUBUNIT, CATFISH

          Enter P or PAGE for more
?p

Ref    Items   RT  Index-term
E13        2       GONADOTROPIN II BETA SUBUNIT, FUNDULUS
E14        3       GONADOTROPIN II, KATSUWONUS
E15        1       GONADOTROPIN II, TUNA
E16        7       GONADOTROPIN INHIBITOR
E17        0    1  GONADOTROPIN RECEPTORS
E18       55       GONADOTROPIN RELEASING HORMONE ASSOCIATED PEPT
E19        0    1  GONADOTROPIN RELEASING-HORMONE RECEPTORS
E20       32       GONADOTROPIN- PITUITARY, BETA-SUBUNIT I, SALMO
E21        5       GONADOTROPIN-ASSOCIATED-PEPTIDE RELEASING ENZY
E22        2       GONADOTROPIN-INHIBITORY HORMONE
E23        0    1  GONADOTROPIN-RELEASING HORMONE
E24        0    1  GONADOTROPIN-RESISTANT OVARY SYNDROME

          Enter P or PAGE for more
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?p

Ref    Items  Index-term
E25     2004  GONADOTROPIN,   BETA  SUBUNIT,  HUMAN  //CHORIONIC  (CHORIONIC
              GONADOTROPIN, BETA SUBUNIT, HUMAN)
E26       45  GONADOTROPIN, PITUITARY, BETA-SUBUNIT II
E27      251  GONADOTROPINA
E28        1  GONADOTROPINABSONDERUNG
E29        2  GONADOTROPINAM
E30        8  GONADOTROPINAMI
E31        1  GONADOTROPINANALYSER
E32        1  GONADOTROPINANTWORT
E33        1  GONADOTROPINAPPLIKATION
E34        1  GONADOTROPINAPPLIKATIONEN
E35       49  GONADOTROPINAS
E36        1  GONADOTROPINAUSCHUTTUNG

          Enter P or PAGE for more
?s gonadotrop?
      S1   54849  GONADOTROP?
?e fsh

Ref    Items   RT  Index-term
E1         1       FSG120KA
E2         1       FSG120KC
E3     20137      *FSH
E4         0    1  FSH (FOLLICLE STIMULATING HORMONE)
E5       825       FSH //RECEPTORS, (RECEPTORS, FSH)
E6         4       FSH BETA
E7         3       FSH PROTEIN
E8         0    1  FSH RECEPTORS
E9         1       FSH-BETA-(33-53)-(81-95)-PEPTIDE AMIDE, HUMAN
E10        2       FSH-BETA-(33-53), HUMAN, SER(51)-
E11        1       FSH-BETA-(81-95), HUMAN, SER(82,84,87,94)-
E12        0    1  FSH-RELEASING HORMONE

          Enter P or PAGE for more
?e e4

Ref    Items Type  RT  Index-term
R1         0        1 *FSH (FOLLICLE STIMULATING HORMONE)
R2     26212   X    9  FOLLICLE STIMULATING HORMONE
?s r1-r2
               0  FSH (FOLLICLE STIMULATING HORMONE)
           26212  FOLLICLE STIMULATING HORMONE
      S2   26212  R1-R2
?e r2

Ref    Items Type  RT  Index-term
R1     26212       9 *FOLLICLE STIMULATING HORMONE
R2     26110   X       DC=D12.644.548.691.525.343.288. (FOLLICLE STIMULATING
                       HORMONE)
R3     26110   X       DC=D6.472.351.576.288. (FOLLICLE STIMULATING HORMONE)
R4     26110   X       DC=D6.472.699.631.525.343.288.  (FOLLICLE STIMULATING
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R5     26110   X       DC=D6.472.734.525.343.288.    (FOLLICLE   STIMULATING
                       HORMONE)
R6         0   X    1  FSH (FOLLICLE STIMULATING HORMONE)
R7       825   R    9  RECEPTORS, FSH
R8      5743   B   17  GONADOTROPINS, PITUITARY
R9       301   N    7  FOLLICLE STIMULATING HORMONE, BETA SUBUNIT
R10      892   N   29  GLYCOPROTEIN HORMONES, ALPHA SUBUNIT
?e r8

Ref    Items Type  RT  Index-term
R1      5743       17 *GONADOTROPINS, PITUITARY
R2      5012   X       DC=D12.644.548.691.525.343. (GONADOTROPINS, PITUITAR-
                       Y)
R3      5012   X       DC=D6.472.351.576. (GONADOTROPINS, PITUITARY)
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R4      5012    X         DC=D6.472.699.631.525.343. (GONADOTROPINS, PITUITARY)
R5      5012    X         DC=D6.472.734.525.343. (GONADOTROPINS, PITUITARY)
R6       223    R    13   RECEPTORS, GONADOTROPIN
R7       234    B    13   FERTILITY AGENTS
R8       698    B    13   FERTILITY AGENTS, FEMALE
R9        43    B     7   FERTILITY AGENTS, MALE
R10    18324    B    13   GONADOTROPINS
R11     2341    B    25   PITUITARY HORMONES, ANTERIOR
R12    26212    N     9   FOLLICLE STIMULATING HORMONE

          Enter P or PAGE for more
?p

Ref    Items Type  RT  Index-term
R13      301   N    7  FOLLICLE STIMULATING HORMONE, BETA SUBUNIT
R14      892   N   29  GLYCOPROTEIN HORMONES, ALPHA SUBUNIT
R15    36107   N   12  LUTEINIZING HORMONE
R16       17   N    8  LUTEINIZING HORMONE, BETA SUBUNIT
R17     2707   N    9  MENOTROPINS
R18    38340   N   11  PROLACTIN
?s r1-r18
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             5012  DC=D6.472.734.525.343.  (GONADOTROPINS, PITUITARY)
              223  RECEPTORS, GONADOTROPIN
              234  FERTILITY AGENTS
              698  FERTILITY AGENTS, FEMALE
               43  FERTILITY AGENTS, MALE
            18324  GONADOTROPINS
             2341  PITUITARY HORMONES, ANTERIOR
            26212  FOLLICLE STIMULATING HORMONE
              301  FOLLICLE STIMULATING HORMONE, BETA SUBUNIT
              892  GLYCOPROTEIN HORMONES, ALPHA SUBUNIT
            36107  LUTEINIZING HORMONE
               17  LUTEINIZING HORMONE, BETA SUBUNIT
             2707  MENOTROPINS
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      S3    87343  R1-R18
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Set     Items   Description
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S2      26212   R1-R2
S3      87343   R1-R18
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            54849  S1
            26212  S2
            87343  S3
      S4   110136  (S1 OR S2 OR S3)
?s s4 and isoform?
           110136  S4
            46261  ISOFORM?
      S5      733  S4 AND ISOFORM?
?s s5 and (disting? or differenti? or identif? or separa? or menopaus?)
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            91320  DISTING?
           630824  DIFFERENTI?
           701054  IDENTIF?
           283332  SEPARA?
            26323  MENOPAUS?
      S6      310  S5 AND (DISTING? OR DIFFERENTI? OR IDENTIF? OR SEPARA? OR
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             5507  EIA
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             49  ELIZA
        2255123  METHOD?
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             34  S8
     S9      75  S7 NOT S8
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             75  S9
          15159  HYBRIDOM?
         167922  MONOCLONAL?
    S10      11  S9 AND (HYBRIDOM? OR MONOCLONAL?)
?t s10/9/all
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10/9/1

DIALOG(R)File 155:MEDLINE(R)

11934626 99378431 PMID: 10451222

Development and characterization of antibodies to a nicked and hyperglycosylated form of hCG from a choriocarcinoma patient: generation of antibodies that differentiate **between pregnancy hCG and choriocarcinoma hCG.**

Birken S; Krichevsky A; O'Connor J; Schlatterer J; Cole L; Kardana A; Canfield R

Department of Medicine, Columbia University College of Physicians and Surgeons, New York, NY 10032, USA. sb18@columbia.edu

Endocrine (UNITED STATES) Apr 1999, 10 (2) p137-44, ISSN 0969-711X Journal Code: 9434444

Contract/Grant No.: AG 13783; AG; NIA; ES 07589; ES; NIEHS; HD 15454; HD; NICHD

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Human chorionic **gonadotropin** (hCG) exists in blood and urine as a variety of **isoforms** one of which contains peptide bond cleavages within its beta-subunit loop 2 and is referred to as nicked hCG (hCGn). This hCG **isoform** appears to be more prevalent in the urine of patients with certain malignancies and possibly in some disorders of pregnancy. Until now, only indirect **immunoassays** could be used to quantify hCGn. We report the development of two **monoclonal** antibodies (MAbs) to a form of hCGn isolated from a choriocarcinoma patient. This hCG **isoform** was not only 100% nicked, but also contained 100% tetrasaccharide-core O-linked carbohydrate moieties in its beta COOH-terminal region. Two-site immunometric **assays** have been developed using these new antibodies, B151 and B152. The former exhibits good specificity for hCGn independent of the source of the hCGn, the form excreted by choriocarcinoma patients or the form of hCGn from normal pregnancies. The latter antibody, B152, is sensitive to the carbohydrate moieties and possibly other differences in hCG **isoforms** , but is not for nicking of the beta-subunit. These two immunometric **assays** provide potential novel diagnostic tools for direct measurement of hCG **isoforms** which could not be accurately quantified earlier before development of the **assays** using these newly generated antibodies.

Tags: Animal; Female; Human; Pregnancy; Support, U.S. Gov't, P.H.S.

Descriptors: Antibodies, **Monoclonal** --chemistry--CH; *Choriocarcinoma --metabolism--ME; *Chorionic **Gonadotropin** --immunology--IM; *Chorionic **Gonadotropin** , beta Subunit, Human--immunology--IM; *Hydatidiform Mole --metabolism--ME; *Peptide Fragments--immunology--IM; *Tumor Markers,

Biological--immunology--IM; *Uterine Neoplasms--metabolism--ME; Antibodies, **Monoclonal** --diagnostic use--DU; Antibodies, **Monoclonal** --immunology--IM ; Antibody Specificity; Down Syndrome--diagnosis--DI; Epitope Mapping; Glycosylation; Mice; Pre-Eclampsia--diagnosis--DI; Radioimmunoassay-- **methods** --MT

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Chorionic Gonadotropin); 0 (Chorionic Gonadotropin, beta Subunit, Human); 0 (Peptide Fragments); 0 (Tumor Markers, Biological); 0 (glycosylated HCG); 0 (urinary gonadotropin fragment)

Record Date Created: 19990928

Record Date Completed: 19990928

10/9/2

DIALOG(R)File 155:MEDLINE(R)

11677750 99113037 PMID: 9895340

Evaluation of nicked human chorionic gonadotropin **content in clinical specimens by a specific immunometric** assay .

Kovalevskaya G; Birken S; Kakuma T; Schlatterer J; O'Connor J F

Irving Center for Clinical Research, Columbia College of Physicians and Surgeons, New York, NY 10032, USA. gk49@columbia.edu

Clinical chemistry (UNITED STATES) Jan 1999, 45 (1) p68-77, ISSN 0009-9147 Journal Code: 9421549

Contract/Grant No.: ESO7589; ES; NIEHS; HD15454; HD; NICHD; M01-RR00645; RR; NCRR

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

We report the development and characterization of an IRMA for the direct measurement of nicked human chorionic **gonadotropin** (hCGn) in blood and urine. hCGn derived from a reference preparation of hCG used as an immunogen elicits **monoclonal** antibodies (mAbs) with enhanced recognition of human luteinizing hormone epitopes. The most specific **assay** for pregnancy hCGn is an IRMA composed of one mAb to choriocarcinoma-derived hCGn (C5) and a second mAb developed from immunization with normal-pregnancy hCGn. This **assay** was used to evaluate hCGn profiles in normal, in vitro fertilization, Down syndrome, and ectopic pregnancies. In all pregnancies, hCGn was usually present in much lower concentrations than the non-nicked hCG **isoform** . Our results suggest that some form of physical **separation** from the overwhelming quantities of non-nicked hCG present in clinical specimens will be required before accurate immunochemical estimations of hCGn can be made.

Tags: Animal; Female; Human; Pregnancy; Support, U.S. Gov't, P.H.S.

Descriptors: Chorionic **Gonadotropin** --blood--BL; *Chorionic **Gonadotropin** --urine--UR; Abortion, Spontaneous--urine--UR; Antibodies, **Monoclonal** --immunology--IM; Antibody Specificity; Biological Markers --blood--BL; Biological Markers--urine--UR; Choriocarcinoma--blood--BL; Choriocarcinoma--urine--UR; Chorionic **Gonadotropin** --immunology--IM; Cross Reactions; Down Syndrome--diagnosis--DI; Fertilization in Vitro; Mice ; Pregnancy, Ectopic--urine--UR; Prenatal Diagnosis; Radioimmunoassay; Uterine Neoplasms--blood--BL; Uterine Neoplasms--urine--UR

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Biological Markers); 0 (Chorionic Gonadotropin)

Record Date Created: 19990128

Record Date Completed: 19990128

10/9/3

DIALOG(R)File 155:MEDLINE(R)

11025115 97378697 PMID: 9234300

Heterogeneity of plasma gonadotropins . **Consequences on immunological properties of LH.**

Roger M; Lalhou N

Hopital Saint-Vincent-de-Paul, Paris, France.
Nuclear medicine and biology (ENGLAND) Apr 1994, 21 (3) p349-57, ISSN 0969-8051 Journal Code: 9304420
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
The pituitary **gonadotropins** FSH and LH are secreted into blood as dimeric glycoproteins which display a wide heterogeneity when submitted to technique of **separation** based on electric charge. That supports the assumption of a major role of the carbohydrates moieties as a source of heterogeneity. No clear difference however has been demonstrated in the biological potency of the different **isoforms** occurring in blood. On the contrary, important discrepancies in immunological activity have been evidenced, mainly as far as LH is concerned. This is particularly important from a practical point of view since some **monoclonal** sandwich **assays** widely used for the measurement of LH levels fail to detect LH in samples from certain subjects. The description of the so-called "invisible LH" phenomenon should prompt international organizations to incite the manufacturers of commercial kits to improve the standardization in **gonadotropin assays** . (30 Refs.)
Tags: Female; Human; Male
Descriptors: **Follicle Stimulating Hormone** --blood--BL; * **Luteinizing Hormone** --blood--BL; **Immunoassay** ; **Luteinizing Hormone** --immunology--IM; Protein Conformation
CAS Registry No.: 9002-67-9 (Luteinizing Hormone); 9002-68-0 (Follicle Stimulating Hormone)
Record Date Created: 19970918
Record Date Completed: 19970918

10/9/4
DIALOG(R)File 155:MEDLINE(R)

10697360 97046606 PMID: 8891527
Interest of epitopic dissection in immunoanalysis of proteins and peptides: review of theoretical and practical aspects.
Niccoli P; Ferrand V; Lejeune P J; Carayon P
Laboratoire de Biochimie Endocrinienne et Metabolique, Institut National de la Sante et de la Recherche Medicale, Faculte de Medecine, Marseille, France.
European journal of clinical chemistry and clinical biochemistry - journal of the Forum of European Clinical Chemistry Societies (GERMANY) Sep 1996, 34 (9) p741-8, ISSN 0939-4974 Journal Code: 9105775
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
The literature abounds with reports showing discrepancies in **immunoassays** of proteins and peptides. Whereas the isomorphism and polymorphism of proteins remains largely hidden in **immunoassays** making use of polyclonal antibodies, the use of **monoclonal** antibodies uncovered the difficulty of accurately **assaying** microheterogeneous analytes. Indeed, most proteic hormones are not entities with unique structures but rather mixtures of molecular forms with slight differences in structure which may reflect large variations in biological and immunological activities; the **monoclonal** antibodies appeared clearly less suited than the polyclonal for testing a mixture of **isoforms** . Protein microheterogeneity also has an impact on **assay** standardisation, since reference preparations may contain several **isoforms** of the analyte. Using recombinant glycoprotein does not solve the problem. Regarding the problem of discrepancy in immunoanalysis of proteins and peptides, we could establish, in a previous work, that discrepancy among lutropin **assay** kits may be related to various causes: i) differences in standard preparation and calibration curves; ii) microheterogeneity of lutropin molecules leading to missing some **isoforms** due to the restricted epitopic

specificity of the **monoclonal** antibodies used in the kits. The epitopic dissection we engaged in appeared thus instrumental in explaining these discrepancies. It allowed us to enumerate epitopes on the surface of lutropin molecules, to elucidate the immunological structure and, finally, to characterize **monoclonal** antibodies used in commercially available lutropin **assay** kits with regard to their epitopic specificity. This work allowed us to interpret the discrepancy in serum lutropin concentration which was related to the use of **monoclonal** antibody with given specificity. Epitopic dissection may thus be instrumental in explaining discrepancy among **immunoassays** of proteins and peptides and in improving the accuracy of kits. (19 Refs.)

Tags: Female; Human; Male; Support, Non-U.S. Gov't

Descriptors: Epitopes--chemistry--CH; * **Immunoassay** -- **methods** --MT; *Peptides--chemistry--CH; *Proteins--chemistry--CH; Antibodies, **Monoclonal** ; Kidney Failure--blood--BL; **Luteinizing Hormone** --blood--BL; **Menopause** --blood--BL; Polycystic Ovary Syndrome--blood--BL; Polymorphism (Genetics); Reagent Kits, Diagnostic--standards--ST; Reference Values

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Epitopes); 0 (Peptides); 0 (Proteins); 0 (Reagent Kits, Diagnostic); 9002-67-9 (Luteinizing Hormone)

Record Date Created: 19970206

Record Date Completed: 19970206

10/9/5

DIALOG(R)File 155:MEDLINE(R)

10576824 96389001 PMID: 8796333

European collaborative study of LH assay **: 3. relationship of immunological reactivity, biological activity and charge of human luteinizing hormone.**

Niccoli P; Costagliola S; Patricot M C; Mallet B; Benahmed M; Carayon P

Laboratoire de Biochimie Endocrinienne et Metabolique, Unite 38 INSERM, Faculte de Medecine, Marseille, France.

Journal of endocrinological investigation (ITALY) May 1996, 19 (5) p260-7, ISSN 0391-4097 Journal Code: 7806594

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

This report describes the results of the third part of the collaborative study organized by a working group sponsored by the Community Bureau of Reference of the European Community Commission. The aim of the present work was to establish the link between immunoreactivity and biological activity of human LH, thus allowing to determine the antigenic domains of the molecule involved in the induction of the biological effect. The relationship between immunoreactivity and electric charge of hLH was also studied. This work allowed to further apprehend hLH isomorphism and its role in discrepancies observed among hLH **assays** and clinical status. It also made the feasibility of measuring biologically active **isoforms** by an immunological **method** to be assessed. The effect of 36 mAb with known epitopic specificity, was evaluated on both hLH binding to rat membrane receptor and hLH induced production of testosterone by porcine Leydig cells. All the epitopes located on the beta subunit were found to be strongly involved in the biological activity whereas 4/9 and 10/18 epitopes present on the alpha subunit or specific for the holomolecule respectively appeared weakly involved. **Assaying** biological hLH using immunological **method** would require that mAb specific for all the epitopes involved in the receptor activation be tested, and thus appears presently unsuitable for routine clinical evaluation. In the previous work some LH **immunoassays** were found to underestimate LH concentrations (J. Endocrinol. Invest 1994, 17: 397-406 and 407-416). The mAb used in liquid phase in these kits were found in the present work to be directed against the domains of LH weakly involved in the activation of the receptor and would suggest that bioactive LH would be misevaluated by these kits. The immunoreactivity of hLH **isoforms** **separated** by isoelectric focusing (IEF) in liquid phase was also determined. IEF allowed to **separate** three groups of hLH **isoforms**

but none of them exhibited a specific discriminating pattern of immunoreactivity when they were tested against a panel of mAb. It suggests that, in our experimental conditions, the electric charge and the immunoreactivity of hLH were not closely linked.

Tags: Animal; Human; Male

Descriptors: **Luteinizing Hormone** --immunology--IM; * **Luteinizing Hormone** --physiology--PH; Antibodies, **Monoclonal** --immunology--IM; Antibody Specificity; Cell Membrane--metabolism--ME; Electrochemistry; Epitopes--analysis--AN; Epitopes--immunology--IM; Epitopes--physiology --PH; **Immunoassay** ; Isoelectric Focusing; Leydig Cells--drug effects--DE; Leydig Cells--metabolism--ME; **Luteinizing Hormone** --pharmacology--PD; Pituitary Gland--chemistry--CH; Rats; Receptors, LH--metabolism--ME; Swine; Testosterone--biosynthesis--BI

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Epitopes); 0 (Receptors, LH); 57-85-2 (Testosterone); 9002-67-9 (Luteinizing Hormone)

Record Date Created: 19970221

Record Date Completed: 19970221

10/9/6

DIALOG(R)File 155:MEDLINE(R)

10568008 96379946 PMID: 8787959

Undetectable luteinizing hormone levels using a monoclonal **immunometric** assay .

Barbe F; Legagneur H; Watrin V; Klein M; Badonnel Y

Service de Biologie Medicale, Maternite Regionale, Nancy, France.

Journal of endocrinological investigation (ITALY) Nov 1995, 18 (10) p806-8, ISSN 0391-4097 Journal Code: 7806594

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Previous studies have shown wide discrepancies among the results obtained with different immunometric **assays** . We present five cases (out of 4000 women) whose plasma luteinizing hormone was not detected using a LH immunometric **assay** (LH Stratus Baxter) but was recognized by other kits. These cases concerned one 28-year-old woman presenting with infertility and four postmenopausal women. The LH Amerlite kit gave detectable but low results. The results obtained with the other kits were > 7 IU/l. FSH levels were > 7 IU/l. In one case, sera were taken before and after the **menopause** ; differences between the LH results increased. Discrepancies among LH **assay** kits have been attributed to variation both in standard curve calibration and in epitope specificity of the kit **monoclonal** antibodies. The Baxter kit might misrecognize some **isoforms** present in postmenopausal women. The present data illustrate the potential false results with such **immunoassays** in routine clinical laboratory testing. When undetectable LH results are not clinically explained or when disparities between LH and FSH are observed, we suggest using a second **methodology** or a bioassay if necessary. Improvement in LH **assays** and standardization might resolve the problem of discrepancies between the LH results.

Tags: Comparative Study; Female; Human

Descriptors: Antibodies, **Monoclonal** ; * **Immunoassay** -- **methods** --MT; * **Luteinizing Hormone** --blood--BL; Adult; False Negative Reactions; **Follicle Stimulating Hormone** --blood--BL; **Immunoassay** --statistics and numerical data--SN; Middle Age; Postmenopause; Reagent Kits, Diagnostic --statistics and numerical data--SN

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Reagent Kits, Diagnostic); 9002-67-9 (Luteinizing Hormone); 9002-68-0 (Follicle Stimulating Hormone)

Record Date Created: 19961021

Record Date Completed: 19961021

10/9/7

DIALOG(R)File 155:MEDLINE(R)

10316762 96118973 PMID: 8581961

Expression of non-muscle myosin isoforms **in rabbit myometrium is estrogen-dependent.**

Chiavegato A; Capriani A; Azzarello G; Vinante O; Pauletto P; Sartore S
Department of Biomedical Sciences, University of Padua, Padua, Italy.

Cell and tissue research (GERMANY) Jan 1996, 283 (1) p7-18, ISSN 0302-766X Journal Code: 0417625
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

The putatative effects of different estrogen levels on the expression of non-muscle myosin **isoforms** in rabbit myometrium have been investigated using three **monoclonal** anti-platelet myosin heavy chain (MyHC) antibodies (NM-F6, NM-G2, and NM-A9). Western blotting analysis of proteolytic digests of human platelet actomyosin indicates that these antibodies are specific for three distinct epitopes. Comparative immunofluorescence tests on cultered human fibroblasts with polyclonal sequence-specific anti-MyHCA antibody suggest that the patterns of NM-F6, NM-.G2 and NM-A9, although similar, do not overlap with that of type-A MyHC. Distribution of NM myosin **isoforms** has been studied in indirect immunofluorescence **assays** using cryosections of tissues from rabbits at various stages of development, pregnancy, or from ovariectomized, 17beta-estradiol-treated ovariectomized, and human chorionic **gonadotropin** -treated animals. Non-muscle myosin antigenicity is still present in the myometrium when the female becomes sexually competent. The immunoreactivity of non-muscle myosin for NM-F6 is steroid-independent, since it does not change with pregnancy or ovariectomy, but that of NM-G2 is estrogen-dependent; the latter disappears during pregnancy and in ovariectomized animals treated with estradiol, whereas it is expressed in ovariectomized rabbits. Although non-muscle myosin immunoreactivity for NM-A9 is detectable under all the experimental conditions, it can assume different patterns of intracellular distribution in vitro (punctate vs filamentous), depending on culture conditions and the presence of estrogens.

Tags: Animal; Female; Human; Pregnancy; Support, Non-U.S. Gov't
Descriptors: *Estrogens--physiology--PH; *Myometrium--metabolism--ME; *Myosins--biosynthesis--BI; Antibodies, **Monoclonal** ; Antibody Specificity; Blotting, Western; Cell **Differentiation** --physiology--PH; Cells, Cultured; Chorionic **Gonadotropin** --pharmacology--PD; Epitope Mapping; Fluorescent Antibody Technique, Indirect; Immunohistochemistry; Isomerism; Muscle, Smooth--cytology--CY; Muscle, Smooth--metabolism--ME; Myometrium --physiology--PH; Myosins--immunology--IM; Ovariectomy; Rabbits
CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Chorionic Gonadotropin); 0 (Estrogens)
Enzyme No.: EC 3.6.1.4 (Myosins)
Record Date Created: 19960319
Record Date Completed: 19960319

10/9/8

07885728 93346545 PMID: 7688376

Variants of human chorionic gonadotropin **from pregnant women and tumor patients recognized by** monoclonal **antibodies.**

Berger P; Schwarz S; Spottl G; Wick G; Mann K
Institute for Biomedical Aging Research, Austrian Academy of Sciences, Innsbruck.

Journal of clinical endocrinology and metabolism (UNITED STATES) Aug 1993, 77 (2) p347-51, ISSN 0021-972X Journal Code: 0375362
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIM; INDEX MEDICUS

In biological fluids, hCG and its free alpha- (hCG alpha) and beta-subunits (hCG beta), occur in multiple forms. These various forms differ at the molecular level primarily in glycosylation, but also differ in protein backbone modifications corresponding to the urinary low molecular weight fragment of the hCG beta-subunit (beta-core fragment). This microheterogeneous nature can be demonstrated by isoelectric focusing in which variants are **separated** into bands with different isoelectric points (pI). To determine whether such isoelectric variants differ in antigenicity and consequently might escape **immunoassay** detection due to overspecificity of **monoclonal** antibodies (MCA), urinary pregnancy hCG (NIH, CR123) and tumor hCG preparations, such as a tumor-specific acidic variant of hCG (hCGav) and the hCG beta-core fragment, were **separated** by isoelectric focusing in the absence or presence of 8 M urea, or by sodium docedyl sulfate-polyacrylamide gel electrophoresis and enzymatically immunostained using an MCA panel directed against 17 different hCG epitopes. MCA against 14 different epitopes accessible on holo-hCG recognized all pI variants of pregnancy holo-hCG or tumor-derived hCGav, as was true for the three MCA recognizing epitopes hidden on holo-hCG but accessible on the free subunits after hCG dissociation by urea. We conclude that each individual pI- **isoform** of holo-hCG and its free subunits expresses the entire set of epitopes recognized by our MCA panel. The carbohydrate moieties that form a biochemical basis for hCG heterogeneity seem to be neither of major antigenic relevance, nor are they structurally related to any particular epitope. Thus, various glycosylation forms of hCG, hCG alpha, hCG beta, and hCG beta-core in normal as well as in pathological samples should safely be detectable and measureable by **immunoassays** employing MCA with appropriate subunit specificity.

Tags: Female; Human; Male; Pregnancy

Descriptors: Antibodies, **Monoclonal** --immunology--IM; *Chorionic **Gonadotropin** --immunology--IM; *Testicular Neoplasms--metabolism--ME; Antibodies, **Monoclonal** --diagnostic use--DU; Blotting, Western; Chorionic **Gonadotropin** --analysis--AN; Chorionic **Gonadotropin** --isolation and purification--IP; Electrophoresis, Polyacrylamide Gel; Epitopes--immunology --IM; Isoelectric Focusing; Testicular Neoplasms--chemistry--CH

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Chorionic Gonadotropin); 0 (Epitopes)

Record Date Created: 19930909

Record Date Completed: 19930909

10/9/9

DIALOG(R)File 155:MEDLINE(R)

07866350 93322032 PMID: 1306849

Prolactin isoforms **secreted by human prolactinomas.**

Hoffmann T; Gunz G; Brue T; Jaquet P; Ronin C

Laboratoire de Neuroendocrinologie Experimentale, INSERM U 297, Marseille, France.

Hormone research (SWITZERLAND) 1992, 38 (3-4) p164-70, ISSN 0301-0163 Journal Code: 0366126

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Prolactin (hPRL) secreted by human prolactinoma cells in culture was purified by gel filtration, lectin affinity chromatography and gel electrophoresis in order to **identify** the different **isoforms** of the hormone and to test their respective immunoreactivities and bioactivities. The nonglycosylated hPRL (NG-hPRL), unbound to lectins, was the major form and was a species (NG1-hPRL), of 23,000 (M(r)) apparent molecular weight. The lectin-bound glycosylated hPRL (G-hPRL) consisted of three forms, G1-, G2- and G3-hPRL, of identical molecular weights (25,000 M(r)). Endoglycosidase treatment indicated that these three forms differed by the heterogeneity of their carbohydrate chains. These G-PRLs proved to be 68% less immunoreactive and 50% less bioactive than NG-hPRL. It is concluded from these data that, in prolactinomas, the main variant of the hormone is the nonglycosylated form of PRL.

Tags: Human; Support, Non-U.S. Gov't
Descriptors: Pituitary Neoplasms--secretion--SE; * **Prolactin** --secretion --SE; *Prolactinoma--secretion--SE; Antibodies, **Monoclonal** ; Cell Division --drug effects--DE; Chromatography, Affinity; Chromatography, Gel; Electrophoresis, Polyacrylamide Gel; Glucosaminidase--metabolism--ME; Glycosylation; Immunoblotting; Immunoradiometric **Assay** ; Isoelectric Focusing; Lymphoma; Molecular Weight; **Prolactin** --isolation and purification--IP; **Prolactin** --pharmacology--PD; Tumor Cells, Cultured
CAS Registry No.: 0 (Antibodies, Monoclonal); 9002-62-4 (Prolactin)
Enzyme No.: EC 3.2.1.- (Glucosaminidase)
Record Date Created: 19930816
Record Date Completed: 19930816

10/9/10

DIALOG(R)File 155:MEDLINE(R)

07787558 93243056 PMID: 8480479

Biological and immunological properties of the international standard for FSH 83/575: isoelectrofocusing profile and comparison with other FSH preparations.

Simoni M; Jockenhovel F; Nieschlag E
Institute of Reproductive Medicine, The University, Munster, Germany.

Acta endocrinologica (DENMARK) Mar 1993, 128 (3) p281-8, ISSN 0001-5598 Journal Code: 0370312
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

The new international standard for FSH, IS 83/575, has been analyzed, after isoelectric focusing **separation** , by Sertoli cell in vitro bioassay, radioligand receptor **assay** and two highly specific immunometric **assays** . Its molecular composition was then compared with the isoelectric focusing profiles obtained from the fractionation of the reference preparation 2nd IRP 78/549 and from pools of human male and female pituitary extracts and male and female sera. The results showed that > 80% of immunoreactive and bioactive FSH in the IS 83/575 has a pI value < 4, while such very acidic material was represented much less in the other FSH preparations tested. All the immunoreactive material contained in the IS 83/575 was shown to be capable of receptor binding and bioactivity in vitro. A generally good correspondence between IEF profiles obtained by bioassay and by immunofluorimetric **assay** was evident in the case of IS 83/575, 2nd IRP 78/549 and pituitary extracts, although the profiles recorded by immunofluorimetric **assay** were rather smooth and more **isoforms** were detected by bioassay. A striking discrepancy between immunoreactive FSH and bioactive FSH was observed after isoelectric focusing fractionation of the serum pools, in which some bioactive material was not detected by immunofluorimetric **assay** and some of the immunoreactive FSH peaks were devoid of bioactivity, indicating that serum contains inhibitors of FSH action and that immunometric **assays** based on **monoclonal** antibodies may miss some bioactive FSH **isoforms** .(ABSTRACT TRUNCATED AT 250 WORDS)

Tags: Comparative Study; Female; Human; In Vitro; Male; Support, Non-U.S. Gov't
Descriptors: **Follicle Stimulating Hormone** --standards--ST; Aged; Aged, 80 and over; Biological **Assay** ; Biological Availability; Fluoroimmunoassay ; **Follicle Stimulating Hormone** --analysis--AN; **Follicle Stimulating Hormone** --chemistry--CH; **Follicle Stimulating Hormone** --pharmacology--PD; Hydrogen-Ion Concentration; Immunoradiometric **Assay** ; Isoelectric Focusing ; Middle Age; Pituitary Gland--metabolism--ME; Radioligand **Assay** ; Receptors, FSH--metabolism--ME; Reference Standards
CAS Registry No.: 0 (Receptors, FSH); 9002-68-0 (Follicle Stimulating Hormone)
Record Date Created: 19930524
Record Date Completed: 19930524

10/9/11

DIALOG(R)File 155:MEDLINE(R)

06968810 91209293 PMID: 2019262

Circulating antagonist of luteinizing hormone in association with infertility in stallions.

Whitcomb R W; Schneyer A L; Roser J F; Hughes J P
Department of Medicine, Massachusetts General Hospital, Boston 02114.

Endocrinology (UNITED STATES) May 1991, 128 (5) p2497-502, ISSN 0013-7227 Journal Code: 0375040
Contract/Grant No.: FD-U-000523-1; FD; FDA; HD-15788; HD; NICHD; HD-25941 ; HD; NICHD
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIM; INDEX MEDICUS

Using a LH radioligand receptor **assay** (RRA) previously validated for use in serum and an equine **monoclonal** RIA, we have **distinguished** a subset of subfertile stallions with an elevated RRA/RIA ratio. After purification of the active moiety by anion exchange chromatography and immunoprecipitation with the equine LH (eLH) **monoclonal** antibody, RRA activity remained in the supernatant. This activity was also recognized by a polyclonal LH antibody (GDN 15) with wide cross-species recognition. This active fraction was further purified by gel filtration chromatography and shown to displace labeled eLH in a dose-dependent fashion in the RRA with an inhibition slope of 2.8 compared with a slope of 1.1 for native eLH. This fraction also inhibited the LH-stimulated steroidogenesis of Leydig cells in vitro in a dose-dependent fashion, but had no effect on basal (minus LH) steroid production. Polyacrylamide gel electrophoresis and electroelution of this material demonstrated RRA activity in a fraction with a mol wt between 45-66 kDa. We conclude that this substance 1) competitively inhibited binding of eLH and hCG to the LH receptor, 2) antagonized LH-stimulated steroidogenesis in vitro, and 3) may represent a LH **isoform** found in association with infertility in these animals.

Tags: Animal; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Descriptors: Horse Diseases--blood--BL; *Horses--blood--BL; *Infertility --veterinary--VE; * **Luteinizing Hormone** --antagonists and inhibitors--AI; Binding, Competitive; Biological **Assay** ; Cell Line; Electrophoresis, Polyacrylamide Gel; Infertility--blood--BL; Leydig Cells--metabolism--ME; **Luteinizing Hormone** --blood--BL; Molecular Weight; Radioimmunoassay; Radioligand **Assay**
CAS Registry No.: 9002-67-9 (Luteinizing Hormone)
Record Date Created: 19910524
Record Date Completed: 19910524

?logoff hold
04jun03 16:25:23 User228206 Session D1981.2
$7.23 2.260 DialUnits File155
$2.31 11 Type(s) in Format 9
$2.31 11 Types
$9.54 Estimated cost File155
$1.16 TELNET
$10.70 Estimated cost this search
$10.70 Estimated total session cost 2.419 DialUnits

Status: Signed Off. (5 minutes)

Status: Path 1 of [Dialog Information Services via Modem]

Status: Initializing TCP/IP using (UseTelnetProto 1 ServiceID pto-dialog)
Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
******** HHHHHHHH SSSSSSSS?
Status: Signing onto Dialog
****

```
ENTER PASSWORD:
 ******** HHHHHHHH SSSSSSSS? ********
Welcome to DIALOG
### Status: Connected


Dialog level 02.14.01D

Reconnected in file 155 04jun03 16:32:04
* * * * See HELP NEWS 225 for information on new search prefixes
and display codes

***                                    ***


File 155:MEDLINE(R)  1966-2003/Jun W1
       (c) format only 2003 The Dialog Corp.
*File 155: Medline has been reloaded and accession numbers have
changed.  Please see HELP NEWS 155.

      Set  Items  Description
      ---  -----  -----------
Cost is in DialUnits
?s s5/2000:2003
             733  S5
         1720182  PY=2000 : PY=2003
     S11     263  S5/2000:2003
?s s5 not s11
             733  S5
             263  S11
     S12     470  S5 NOT S11
?s s12 and sial?
             470  S12
           29610  SIAL?
     S13      27  S12 AND SIAL?
?ds

Set     Items   Description
S1      54849   GONADOTROP?
S2      26212   R1-R2
S3      87343   R1-R18
S4     110136   (S1 OR S2 OR S3)
S5        733   S4 AND ISOFORM?
S6        310   S5 AND (DISTING? OR DIFFERENTI? OR IDENTIF? OR SEPARA? OR -
                MENOPAUS?)
S7        109   S6 AND (ASSAY? OR IMMUNOASSAY? OR EIA OR ELISA OR ELIZA OR
                METHOD?)
S8         34   S7/2000:2003
S9         75   S7 NOT S8
S10        11   S9 AND (HYBRIDOM? OR MONOCLONAL?)
S11       263   S5/2000:2003
S12       470   S5 NOT S11
S13        27   S12 AND SIAL?
?s s13 not s10
              27  S13
              11  S10
     S14      27  S13 NOT S10
?t s14/9/all

 14/9/1
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

11999756   99445408   PMID: 10514553
   Oestrogens regulate pituitary alpha2,3- sialyltransferase messenger
ribonucleic acid levels in the female rat.
  Damian-Matsumura  P; Zaga V; Maldonado A; Sanchez-Hernandez C; Timossi C;
Ulloa-Aguirre A
  Department  of  Reproductive  Biology, Instituto Nacional de la Nutricion
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Salvador Zubiran, Mexico.
Journal of molecular endocrinology (ENGLAND) Oct 1999, 23 (2) p153-65, ISSN 0952-5041 Journal Code: 8902617
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Follicle-stimulating hormone (FSH) is synthesized by the anterior pituitary gland in multiple molecular forms. Increased acidic/ **sialylated** FSH charge **isoforms** are associated with conditions characterized by a low oestrogen output. In the present study, we analysed the dynamics of the changes in mRNA levels of the enzyme Galbeta1,3[4]GlcNAc alpha2,3- **sialyltransferase** (2,3-STase) (one of the enzymes that incorporate **sialic** acid residues into the FSH molecule) in intact and ovariectomized rats. The anterior pituitaries of 4-day regularly cyclic adult female Wistar rats were obtained at 1000 h on the days of pro-oestrus (P), oestrus (O), dioestrus 1 (D1) and dioestrus 2 (D2), at 0200 h, 1400 h, 1800 h and 2200 h on D1, at 1800 h on day of O and at 1000 h after 7, 14, 21, 28 and 45 days of oophorectomy performed on the morning of P. Total RNA was isolated from each gland and the 2,3-STase levels were measured by Northern blot hybridization analysis employing a 346-base pair cDNA probe encoding for a non-conserved amino acid sequence of the catalytic domain of the enzyme. Maximal levels of the enzyme mRNA were detected at 1000 h on D1; thereafter, they progressively decreased by 60% during the ensuing 24 h, reaching the lowest concentration values (26% of the maximally observed level on D1) at 1000 h on day of P and remaining unchanged during the morning of O. Administration of the potent oestradiol receptor antagonist ICI 182,780 at 1000 h on D1 completely reverted the time-dependent decrease in 2,3-STase mRNA levels observed during the afternoon of D1, whereas oestradiol benzoate administered at 1000 h on day of O significantly reduced the enzyme mRNA levels (to 21% of the levels detected in vehicle-treated controls). In ovariectomized rats, the alpha2,3-STase mRNA progressively increased from day 21 to day 45 post castration. Administration of oestradiol benzoate on day 28 after oophorectomy significantly reduced the 2,3-STase mRNA levels (to 36% of the levels detected in vehicle-injected controls); ICI 182,780 partially counteracted this oestradiol-mediated effect. The dynamics of these changes in 2,3-STase mRNA levels partially correlated with changes in the relative abundance of the FSH charge **isoforms** separated by preparative chromatofocusing of anterior pituitary extracts, particularly in glands obtained during the morning of P and O. These data demonstrate for the first time that pituitary 2,3-STase is a hormonally-regulated enzyme and that the changes in transcription and/or stability of its mRNA may be involved, in part, in the post-translational processing of the FSH molecule during certain physiological conditions.

Tags: Animal; Female; Support, Non-U.S. Gov't

Descriptors: Estrogens--physiology--PH; *Gene Expression Regulation, Enzymologic--physiology--PH; *Pituitary Gland, Anterior--enzymology--EN; *RNA, Messenger--genetics--GE; * **Sialyltransferases** --genetics--GE; Base Sequence; DNA, Complementary; Estradiol--blood--BL; **Follicle Stimulating Hormone** --blood--BL; Rats; Rats, Wistar

CAS Registry No.: 0 (DNA, Complementary); 0 (Estrogens); 0 (RNA, Messenger); 50-28-2 (Estradiol); 9002-68-0 (Follicle Stimulating Hormone)

Enzyme No.: EC 2.4.99.- (**Sialyltransferases**); EC 2.4.99.4 (beta-galactoside alpha-2,3- **sialyltransferase**)

Record Date Created: 20000210
Record Date Completed: 20000210

14/9/2
DIALOG(R)File 155:MEDLINE(R)

11934623 99378428 PMID: 10451219

Receptor binding activity and in vitro biological activity of the human FSH charge isoforms **as disclosed by heterologous and homologous assay systems: implications for the structure-function relationship of the FSH**

variants.

Zambrano E; Zarinan T; Olivares A; Barrios-de-Tomasi J; Ulloa-Aguirre A
Department of Reproductive Biology, Instituto Nacional de la Nutricion Salvador Zubiran, Mexico DF, Mexico.

Endocrine (UNITED STATES) Apr 1999, 10 (2) p113-21, ISSN 0969-711X Journal Code: 9434444
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Follicle-stimulating hormone (FSH) is produced and secreted in multiple molecular forms. These **isoforms** differ in their oligosaccharide structures, which determine the particular behavior of a given variant in in vitro and in vivo systems. Employing heterologous cell assay systems, this and other laboratories have shown that highly **sialylated** human FSH variants exhibit lower receptor binding/immunoactivity as well as in vitro bioactivity/immunoactivity relationships than their less **sialylated** counterparts. It is not known, however, whether this characteristic behavior of the FSH **isoforms** is reproduced by homologous assay systems, in which unique variants of the receptor are presumptively expressed. To gain further insights into the structure-activity relationship of the various FSH **isoforms** , we analyzed the capacity of nine charge **isoforms** obtained after high-resolution chromatofocusing (pH window, 7.10 to <3.80) of anterior pituitary glycoprotein extracts to bind and activate their cognate receptor expressed by naturally occurring heterologous cell systems (rat granulosa cells and seminiferous tubule homogenates) as well as by human embryonic kidney-derived 293 (HEK-293) cells transfected with the human FSH (FSH-R) receptor cDNA. In both (heterologous and homologous) receptor assay systems, the **isoforms** displaced 125I-labeled FSH from the receptor in a dose-response manner; however, whereas in the heterologous systems, the receptor binding activity varied according to the elution pH value/ **sialic** content of the **isoforms** , with the less acidic variants exhibiting higher receptor binding activity ($r = 0.851$ and 0.495 [$p < 0.01$ and $p < 0.05$] for the granulosa cell and testicular homogenate receptor assay systems, respectively) than the more acidic/ **sialylated** analogs, in the homologous assay, this relationship was practically absent ($r = 0.372$, p N.S.). The capacity of the **isoforms** to induce androgen aromatization by rat granulosa cells followed the same trend shown by its corresponding receptor assay system ($r = 0.864$, $p < 0.01$). Interestingly and in contrast to the results observed in the homologous receptor binding assay, the ability of the **isoforms** to induce cAMP production by HEK-293 cells varied according to their elution pH value, with the more **sialylated** **isoforms** exhibiting lower potency than their less acidic counterparts ($r = 0.852$, $p < 0.01$). The results yielded by the heterologous assays suggest that the different potency of the **isoforms** to elicit a biological effect in a naturally occurring receptor system depends primarily on the particular affinity of the receptor molecule for each **isoform** . The existence of a clear dissociation between receptor binding and signal transduction in the homologous system indicate that this later function is rather related to the different ability of the FSH glycosylation variants to induce and/or stabilize distinct receptor conformations that may permit preferential or different degrees of activation/inhibition of a given signal transduction pathway. Thus, the human FSH receptor-transducer system apparently possesses sufficient versatility to respond in a different manner to glycosylation-dependent diverse FSH signals.

Tags: Animal; Female; Human; Support, Non-U.S. Gov't
Descriptors: **Follicle Stimulating Hormone** --metabolism--ME; *Receptors, FSH--metabolism--ME; Cells, Cultured; Chromatography, Ion Exchange; Cyclic AMP--metabolism--ME; Granulosa Cells--metabolism--ME; Hydrogen-Ion Concentration; Kinetics; Pituitary Gland--metabolism--ME; Protein Binding; Radioimmunoassay; Rats; Signal Transduction
CAS Registry No.: 0 (Receptors, FSH); 60-92-4 (Cyclic AMP); 9002-68-0 (Follicle Stimulating Hormone)
Record Date Created: 19990928
Record Date Completed: 19990928

DIALOG(R)File 155:MEDLINE(R)

11822914 99262697 PMID: 10325254
Biological characterization of recombinant human follicle stimulating hormone isoforms .
D'Antonio M; Borrelli F; Datola A; Bucci R; Mascia M; Polletta P; Piscitelli D; Papoian R
Istituto di Ricerca C.Serono SpA, Via Valle Caia 22, I-00040 Ardea (Rome), Italy.
Human reproduction (Oxford, England) (ENGLAND) May 1999, 14 (5) p1160-7, ISSN 0268-1161 Journal Code: 8701199
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
It has been established that follicle stimulating hormone (FSH) circulates in the bloodstream as a heterogeneous population of molecules. Individual FSH **isoforms** , while displaying identical amino acid sequences, differ in their extent of post-translational modification. As a result of these variations, the FSH **isoforms** exhibit differences in overall charge, degree of **sialic** acid or sulphate incorporation, receptor binding affinity and plasma half-life. Taking advantage of the fact that these forms can be separated from each other on the basis of their charge, we have evaluated in rats the metabolic clearance rates of the acidic [with an isoelectric point (pI) </=ISOdia</= 4.8] and the less acidic (pI > 4.8) **isoforms** of recombinant human FSH (rhFSH) obtained after chromatofocusing. The less acidic **isoform** group was found to have a faster clearance from the circulation in rats as compared with the acidic **isoform** group. This finding is in agreement with the lower bioactivity in vivo (as determined by the Steelman-Pohley assay) of the less acidic **isoform** group, compared with the acidic one. The mass spectra of the two groups of **isoforms** showed a difference in the **sialic** acid content thus highlighting the importance of these residues on the in-vivo activity of FSH. Conversely, when the two groups of **isoforms** were tested in vitro by using the Y1 human FSH receptor (Y1 hFSHR) assay and a reporter gene assay, no significant differences in the biological activities between these preparations were detected when test concentrations were based on mass.
Tags: Animal; Human
Descriptors: **Follicle Stimulating Hormone** --chemistry--CH; *Protein **Isoforms** --chemistry--CH; Biological Assay; CHO Cells; **Follicle Stimulating Hormone** --metabolism--ME; **Follicle Stimulating Hormone** --pharmacokinetics--PK; Genes, Reporter; Half-Life; Hamsters; Isoelectric Focusing; Metabolic Clearance Rate; Protein **Isoforms** --metabolism--ME; Protein **Isoforms** --pharmacokinetics--PK; Rats; Rats, Sprague-Dawley; Recombinant Proteins--chemistry--CH; Recombinant Proteins--metabolism--ME; Recombinant Proteins--pharmacokinetics--PK; Spectrum Analysis, Mass
CAS Registry No.: 0 (Protein Isoforms); 0 (Recombinant Proteins); 9002-68-0 (Follicle Stimulating Hormone)
Record Date Created: 19990714
Record Date Completed: 19990714

14/9/4
DIALOG(R)File 155:MEDLINE(R)

11667156 99102186 PMID: 9882548
Changes in levels of immunoreactive prolactin isoforms **during a reproductive cycle in turkey hens.**
Bedecarrats G; Guemene D; Kuhnlein U; Zadworny D
Department of Animal Science, McGill University, Ste Anne de Bellevue, Quebec, H9X 3V9, Canada.
General and comparative endocrinology (UNITED STATES) Jan 1999, 113 (1) p96-104, ISSN 0016-6480 Journal Code: 0370735
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM

Record type: Completed
Subfile: INDEX MEDICUS

Changes in the ratio between immunoreactive **isoforms** of **prolactin** using Western blotting and in the total **prolactin** content using radioimmunoassay were measured in pituitary glands from turkey hens at different physiological stages. The type of glycosylation (N- or O-linked carbohydrates) was determined using endoglycosidase digestion (N-glycosidase F, O-glycosidase, and neuraminidase). Low levels of **prolactin** were observed in pituitary glands from sexually immature, out-of-lay, and molting hens. Higher levels were present during the egg-laying period and the highest levels were detected in hens which expressed incubation behavior. Two immunoreactive bands of apparent molecular weights of 24 and 27 kDa were visualized on Western blots, corresponding to the nonglycosylated and glycosylated forms of **prolactin** , respectively. In pituitary glands from incubating turkey hens, about 70% of the **prolactin** was glycosylated (27-kDa **isoforms**), whereas about 60% was glycosylated in immature and in hens during the first egg-laying period. In pituitaries from out-of-lay and molting hens the percentage of glycosylated **prolactin** was 38 and 33%, respectively. Thus, higher percentages of glycosylated **isoforms** (27 kDa) were associated with high levels of total **prolactin** and lower percentages were associated with low levels of **prolactin** content in the pituitary gland. Digestion of the **isoforms** with N-glycosidase F resulted in a single band with an apparent molecular weight of 24 kDa. Partial deglycosylation was achieved using neuraminidase, whereas digestion with O-glycosidase had no apparent effect on the **isoforms** . Thus it appears that the glycosylated **isoforms** of **prolactin** have N-linked carbohydrates containing **sialic** acid. Copyright 1999 Academic Press.

Tags: Animal; Female; Support, Non-U.S. Gov't

Descriptors: Menstrual Cycle--physiology--PH; * **Prolactin** --blood--BL; *Turkeys--metabolism--ME; Blotting, Western; Glucose--analysis--AN; Isomerism; Photic Stimulation; Pituitary Gland--chemistry--CH; **Prolactin** --analysis--AN; Prostaglandins E; Radioimmunoassay

CAS Registry No.: 0 (Prostaglandins E); 50-99-7 (Glucose); 9002-62-4 (Prolactin)

Record Date Created: 19990303

Record Date Completed: 19990303

14/9/5

DIALOG(R)File 155:MEDLINE(R)

11202167 98078788 PMID: 9418979

Effect of desialylation of highly purified isoforms **of human luteinizing hormone on their bioactivity in vitro, radioreceptor activity and immunoactivity.**

Burgon P G; Stanton P G; Pettersson K; Robertson D M

Prince Henry's Institute of Medical Research, Monash Medical Centre, Clayton, Vic., Australia.

Reproduction, fertility, and development (AUSTRALIA) 1997, 9 (5) p501-8, ISSN 1031-3613 Journal Code: 8907465

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

To establish whether **sialic** acid content is responsible for an observed 7-8-fold variability in bioactivity in vitro of highly purified human pituitary luteinizing hormone (hLH) **isoforms** , the bioactivity in vitro, radioreceptor activity and immunoactivity of hLH **isoforms** were determined before and after enzymatic desialylation. Three immunofluorometric assays with different hLH specificities allowed characterization of 13-24 pituitary hLH **isoform** preparations of pI 7.03-8.98 in terms of **sialic** acid content (1-5 **sialic** acid residues per LH molecule), bioactivity in vitro (4030-30,000 I.U. mg[-1]), radioreceptor activity (6420-25,400 I.U. mg[-1]) and hLH immunoactivity (2900-4400 to 18,300-27,300 I.U. mg[-1]). Significant positive correlations between **sialic** acid content and either immunoactivity or in vitro bioactivity were observed, whereas radioreceptor

activity showed a curvilinear response. Following more than 90% removal of **sialic** acid, both in vitro bioactivity and radioreceptor activity were increased, although specific activity still differed between **isoforms** ; immunoactivities were unaffected. It is concluded that the presence of the **sialic** acid residue(s) on hLH **isoforms** does partially contribute to the in vitro bioactivity and radioreceptor activity of the **isoforms** , but that hLH immunoactivity is independent of **sialic** acid content.

Tags: Animal; Comparative Study; Human; Support, Non-U.S. Gov't

Descriptors: **Luteinizing Hormone** --chemistry--CH; * **Luteinizing Hormone** --metabolism--ME; *N-Acetylneuraminic Acid--analysis--AN; Biological Assay; Electrophoresis, Polyacrylamide Gel; Fluoroimmunoassay; **Luteinizing Hormone** --immunology--IM; **Luteinizing Hormone** --isolation and purification--IP; Mice; Neuraminidase--metabolism--ME; Radioligand Assay; Sensitivity and Specificity

CAS Registry No.: 131-48-6 (N-Acetylneuraminic Acid); 9002-67-9 (Luteinizing Hormone)

Enzyme No.: EC 3.2.1.18 (Neuraminidase)

Record Date Created: 19980217

Record Date Completed: 19980217

14/9/6

DIALOG(R)File 155:MEDLINE(R)

11027788 97381373 PMID: 9238705

Molecular biology and biochemistry of human recombinant follicle stimulating hormone (Puregon).

Olijve W; de Boer W; Mulders J W; van Wezenbeek P M

NV Organon, Oss, The Netherlands.

Molecular human reproduction (ENGLAND) May 1996, 2 (5) p371-82, ISSN 1360-9947 Journal Code: 9513710

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Follicle stimulating hormone (FSH) is a heterodimeric glycoprotein hormone produced in the anterior pituitary gland. The hormone is essential in the regulation of reproductive processes, such as follicular development and ovulation. It is clinically used for treatment of anovulation and in assisted reproduction technologies such as in-vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI). Until recently, the only source for human FSH has been the urine from post-menopausal women. Such a natural source implies limited availability and potential product variability. Thus, we have cloned the genes encoding the alpha- and beta-subunits of human FSH and transfected these into Chinese hamster ovary (CHO) cells. A CHO-clone was isolated capable of secreting intact glycosylated FSH with identical amino acid sequences to natural FSH. This cell line was grown in perfusion culture and enabled us to isolate highly pure FSH (> 99%). The complexity of the charge distribution of human recombinant FSH was demonstrated by Isoelectric focusing. The observed microheterogeneity is caused by the large number of carbohydrate chain structures which are added to the four potential glycosylation sites in the alpha beta-dimer. Furthermore, the carbohydrates show a variation in their degree of **sialylation** which reflects the different pl values of the individual isohormones. Despite the complexity of post-translational modification, the **isoform** distribution of recombinant FSH produced in a CHO-cell line and grown in perfusion culture is surprisingly similar to that observed with pituitary FSH and urinary FSH. In conclusion, we have shown that FSH-gene transfected CHO-cells are capable of stable serum-free production of recombinant FSH. A process has been developed which assures the consistent and reproducible production of highly-purified recombinant FSH. (46 Refs.)

Tags: Animal; Female; Human

Descriptors: **Follicle Stimulating Hormone** ; **Follicle Stimulating Hormone** --genetics--GE; **Follicle Stimulating Hormone** --metabolism--ME; Hamsters; Recombinant Proteins--genetics--GE; Recombinant Proteins --metabolism--ME

CAS Registry No.: 0 (Recombinant Proteins); 9002-68-0 (Follicle

Stimulating Hormone)
Record Date Created: 19970902
Record Date Completed: 19970902

14/9/7
DIALOG(R)File 155:MEDLINE(R)

10840288 97191557 PMID: 9039515
Altered follicle stimulating hormone isoforms **in female galactosaemia patients.**
Prestoz L L; Couto A S; Shin Y S; Petry K G
INSERM U394 Neurobiologie integrative, Bordeaux, France.
European journal of pediatrics (GERMANY) Feb 1997, 156 (2) p116-20, ISSN 0340-6199 Journal Code: 7603873
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Many women affected with galactosaemia suffer from ovarian dysfunction and have elevated serum levels of follicle stimulating hormone (FSH). We have analysed FSH-glycoprotein **isoforms** from four galactosaemic and five healthy women. Besides the commonly found FSH species with a median isoelectric point (pI) of 4-5, the sera of the female galactosaemic patients contained qualitatively abnormal FSH **isoforms** with a pI close to neutral (6.4-7.0). The generally reduced galactosylation in patient samples was confirmed because sera of galactosaemic patients could incorporate 1.7 times more UDP-(14C)galactose than did healthy subjects. Conclusion: Our data indicate that the terminal disaccharides of FSH (a glycoprotein), galactose and **sialic** acid were partially deficient in three galactosaemic female patients with no galactose-1-phosphate uridyl transferase (GALT) activity in red cells. However, from a female patient with a residual GALT activity (a mild form of galactosaemia), no distinctive deficiency was observed. This again suggest an importance of GALT in retaining a correct FSH structure. Therefore the abundance of neutral FSH **isoforms** , which was described to have a higher binding affinity to its receptor and no capacity to activate cyclic adenosine mono-phosphate (cAMP), may cause a hormonal dysfunction in classical galactosaemia.
Tags: Female; Human; Support, Non-U.S. Gov't
Descriptors: **Follicle Stimulating Hormone** --analysis--AN; *Galactosemias --blood--BL; Adolescent; Adult; Child; Immunoblotting; Isoelectric Focusing
CAS Registry No.: 9002-68-0 (Follicle Stimulating Hormone)
Record Date Created: 19970415
Record Date Completed: 19970415

14/9/8
DIALOG(R)File 155:MEDLINE(R)

10828028 97179064 PMID: 9027351
Structural and functional characterisation of hFSH and hLH isoforms .
Stanton P G; Burgon P G; Hearn M T; Robertson D M
Prince Henry's Institute of Medical Research, Clayton, Victoria, Australia.
Molecular and cellular endocrinology (IRELAND) Dec 20 1996, 125 (1-2) p133-41, ISSN 0303-7207 Journal Code: 7500844
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Human follicle-stimulating hormone (hFSH) and luteinizing hormone (hLH) are **gonadotropins** which are secreted as multiple forms by the pituitary. Evidence supporting the structural and functional heterogeneity of 15 purified hFSH **isoforms** and 20 purified hLH **isoforms** from pituitary extracts will be presented. **Gonadotropin isoforms** were purified by a

combination of preparative isoelectric focusing and ion-exchange chromatography. The protein mass of each **isoform** was determined by amino acid analysis, which also correlated (data for hLH) ($r = 0.999$, $P < 0.001$, $n = 15$) with the UV area under the curve at 280 nm of the **isoforms** following gel-filtration HPLC. The alpha and beta subunits of FSH and LH were shown to be intact by SDS-PAGE under reducing condition, with no evidence of proteolytic nicking or presence of contaminating proteins. hFSH radioreceptor activity varied over a seven-fold range, and a positive correlation ($r = 0.85$, $P < 0.001$, $n = 9$) was observed between FSH receptor activity and the **sialic** acid (SA) content (1.5-13.7 mol SA/mol hFSH) of the **isoforms** , as determined by an HPLC-based microfluorometric assay. FSH in vitro activities varied over a similar range with a high correlation ($r = 0.82$, $n = 15$) with receptor activities, suggesting that the initial association of the hormone with the receptor is the key interaction with less differences attributed to subsequent effects in the signaling pathway. A similar result was seen with the hLH **isoforms** . To explore FSH/LH in vivo, the circulating half-life (LH/FSH) and the in vivo bioactivity (LH) using an acute in vivo assay was investigated. The clearance of hLH and hFSH showed a bi-exponential pattern for all **isoform** preparations with the proportion of the slower dissociating component (t 1/2 50-60 min) increasing three-fold with increasing **sialic** acid content of the **isoform** . The more rapidly cleared component (t 1/2 approx 10 min) is attributed to hepatically cleared **gonadotropin** , rather than **gonadotropin** equilibration between body compartments. The in vivo assay procedure for LH was based on the 24 h integrated plasma testosterone levels in rats following administration of graded doses of hLH **isoform** or standard. A 16-fold range in vivo activities between LH **isoforms** ($n = 14$) was observed. A comparison between hLH in vitro and in vivo activities showed a good correlation ($r = 0.75$) with the slope of the regression line (1.39) not significantly different from unity. These results suggest that in this acute in vivo assay method, the differences in circulating half-lives between hLH **isoforms** although large is not a key factor in their in vivo activity. However, in chronic in vivo assay systems the differences in clearance rates between **isoforms** may be important in their subsequent biological response. It is concluded that structural heterogeneity of FSH and LH contributes to functional differences, with a key interaction occurring at the receptor level. The contribution of **sialic** acid to these activities was also investigated. (31 Refs.)

Tags: Animal; Human

Descriptors: **Follicle Stimulating Hormone** --chemistry--CH; * **Follicle Stimulating Hormone** --physiology--PH; * **Luteinizing Hormone** --chemistry--CH ; * **Luteinizing Hormone** --physiology--PH; **Follicle Stimulating Hormone** --isolation and purification--IP; **Follicle Stimulating Hormone** --pharmacology--PD; Half-Life; **Luteinizing Hormone** --isolation and purification--IP; **Luteinizing Hormone** --pharmacology--PD; N-Acetylneurami nic Acid--analysis--AN; Structure-Activity Relationship

CAS Registry No.: 131-48-6 (N-Acetylneuraminic Acid); 9002-67-9 (Luteinizing Hormone); 9002-68-0 (Follicle Stimulating Hormone)

Record Date Created: 19970417

Record Date Completed: 19970417

14/9/9

DIALOG(R)File 155:MEDLINE(R)

10701368 97050625 PMID: 8895353

In vivo bioactivities and clearance patterns of highly purified human luteinizing hormone isoforms .

Burgon P G; Stanton P G; Robertson D M

Prince Henry's Institute of Medical Research, Clayton, Victoria, Australia.

Endocrinology (UNITED STATES) Nov 1996, 137 (11) p4827-36, ISSN 0013-7227 Journal Code: 0375040

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

Previous studies have shown that highly purified **isoforms** of human pituitary LH exhibited a 20-fold range of in vitro bioactivities. The aim of this study was to determine the corresponding plasma half-lives, metabolic clearance rates (MCR), and in vivo bioactivities of these human (h) LH **isoforms** . Cannulated adult male rats were administered hLH **isoforms** as a bolus i.v. injection. For the half-life studies, blood was then serially collected over a 6-h period, and serum was assayed for hLH using a specific immunofluorometric assay. All hLH (n = 19) **isoforms** exhibited biexponential disappearance profiles with an initial fast half-life (t 1/2) for component A of 12.8 +/- 3.7 min, followed by a slow component B with t 1/2 of 58.9 +/- 4.4 min. The prevalence of component B in relation to component A increased significantly (r = 0.81, P < 0.001) over a 3-fold range when correlated with the **sialic** acid content of the **isoform** . Similarly, the MCR showed a significant correlation (r = 0.77, P < 0.001) with **sialic** acid content. The basis for the two t 1/2 components was then investigated. In the first experiment, rat plasma containing primarily component B was collected 90 min after hLH **isoform** administration and injected into a second animal. Only component B was observed with no evidence of component A, which indicates that the two t 1/2 components are not the product of the redistribution of the hLH **isoform** between body compartments. In the second experiment, component B was found to be dependent on **sialic** acid content, as desialylated hLH **isoforms** showed a rapid disappearance (t 1/2 = 8.6 +/- 3.1) with the component B proportion decreasing to < 10% of that of the nondesialylated control. This data indicates that **sialic** acid protects component B from rapid clearance. In addition, the proportion of the two components is dependent on **sialic** acid content, suggesting that the molecular location of the **sialic** acid on the carbohydrate moieties of hLH has a critical role in the clearance process. To determine the in vivo bioactivity of the hLH **isoforms** , an acute in vivo bioassay was developed in male rats. The assay was based on the hLH dose-dependent increase in total testosterone release in the same rat model as used in the plasma disappearance studies. Using the second International Standard (IS) hLH (0.3 IU-2.6 IU/kg) as standard, a linear dose-response of 24-h integrated serum testosterone levels was observed, with an index of precision of 0.11. Using this in vivo assay, a 16-fold range in in vivo bioactivities (3,200 to 51,100 IU/mg) was observed for 14 hLH **isoforms** . These in vivo bioactivities correlated with **sialic** acid content (r = 0.78, P < 0.001), MCR (r = 0.56, P < 0.05) and LH in vitro bioactivity (r = 0.75, P < 0.001) as determined using mouse Leydig cells in culture. Desialylation lead to over a 100-fold decrease in in vivo bioactivity of hLH. It is concluded that hLH **isoforms** are cleared in vivo by a two-component clearance mechanism, the proportion of which varies between **isoforms** and is dependent on **sialic** acid content of the **isoform** . These findings suggest that the molecular location of **sialic** acid on the hLH **isoform** is critical in defining the plasma disappearance of component B, whereas the mechanism of elimination of component A may well involve the hepatic GalNAc-sulphate receptor. Using an in vivo bioassay, the 16-fold difference in bioactivity between **isoforms** is attributed primarily to differences in their in vitro activity at the cellular level with a minor influence (< 2-fold) due to differences in in vivo clearance.

Tags: Animal; Female; Human; Male; Support, Non-U.S. Gov't

Descriptors: **Luteinizing Hormone** --pharmacokinetics--PK; * **Luteinizing Hormone** --pharmacology--PD; Biological Assay; Chromatography, High Pressure Liquid; Glycosylation; Half-Life; Leydig Cells--drug effects--DE; Leydig Cells--metabolism--ME; **Luteinizing Hormone** --analogs and derivatives--AA; **Luteinizing Hormone** --isolation and purification--IP; Metabolic Clearance Rate; Mice; N-Acetylneuraminic Acid--analysis--AN; Pituitary Gland, Anterior--chemistry--CH; Rats; Rats, Sprague-Dawley; Regression Analysis; Testosterone--blood--BL; Testosterone--metabolism--ME

CAS Registry No.: 131-48-6 (N-Acetylneuraminic Acid); 57-85-2 (Testosterone); 9002-67-9 (Luteinizing Hormone)

Record Date Created: 19961217

Record Date Completed: 19961217

14/9/10

10697361 97046607 PMID: 8891528

Glycosylation is the structural basis for changes in polymorphism and immunoreactivity of pituitary glycoprotein hormones.

Zerfaoui M; Ronin C

UPR 9024 CNRS, Marseille, France.

European journal of clinical chemistry and clinical biochemistry - journal of the Forum of European Clinical Chemistry Societies (GERMANY) Sep 1996, 34 (9) p749-53, ISSN 0939-4974 Journal Code: 9105775

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Glycoprotein hormones have long been known to display extensive polymorphism and changes in bioactivity according to the endocrine status of the patient. Structural analysis has shown that pituitary **gonadotropins** (lutropin and follitropin) and thyrotropin are synthesized and secreted as a panel of **isoforms** which differ in glycosylation, bioactivity and circulatory half-life. Ultrasensitive immunoassays could reveal that glycosylation of plasma hormones is structurally different from the pituitary stock so that the ratio of circulating glycoforms may vary according to the physiopathology of the pituitary axis. However, contradictory results between immunoassays have been often reported, suggesting that some plasma forms can escape recognition by monoclonal antibodies which have been raised to the pituitary or urinary antigen. When hormone levels do not correlate with clinical features, one can also suspect that inactive or hyperactive forms are being measured. At the molecular level, very limited information has been gained toward the expression of hormone epitopes as a function of carbohydrate structure. To address this issue, we have compared the recognition of pituitary and recombinant human thyrotropin by various polyclonal and monoclonal antibodies before and after neuraminidase treatment. Both, pituitary and recombinant thyrotropin bound to anti-alpha and anti-beta antibodies, demonstrating thereby that recombinant thyrotropin can be used to calibrate immunoassays. While removal of **sialic** acid did not alter the recognition of the recombinant hormone in various immunoassays, this treatment specifically abolished the binding of pituitary thyrotropin to anti-beta monoclonal antibodies. These findings show that immunoreactivity of circulating hormone glycoforms, which are often more **sialylated** than their pituitary counterparts, may very well account for variation depending on the antibodies used in the immunoassays. (12 Refs.)

Tags: Human

Descriptors: *Pituitary Hormones--chemistry--CH; *Pituitary Hormones --genetics--GE; *Polymorphism (Genetics); Chorionic **Gonadotropin** --chemistry--CH; Chorionic **Gonadotropin** --genetics--GE; **Follicle Stimulating Hormone** --chemistry--CH; **Follicle Stimulating Hormone** --genetics--GE; Glycoproteins--chemistry--CH; Glycoproteins--genetics--GE; Glycosylation; Immunoassay; Isoelectric Focusing; **Luteinizing Hormone** --chemistry--CH; **Luteinizing Hormone** --genetics--GE; Pituitary Hormones --immunology--IM; Recombinant Proteins--chemistry--CH; Thyrotropin --chemistry--CH; Thyrotropin--genetics--GE

CAS Registry No.: 0 (Chorionic Gonadotropin); 0 (Glycoproteins); 0 (Pituitary Hormones); 0 (Recombinant Proteins); 9002-67-9 (Luteinizing Hormone); 9002-68-0 (Follicle Stimulating Hormone); 9002-71-5 (Thyrotropin)

Record Date Created: 19970206

Record Date Completed: 19970206

14/9/11

10682748 97031915 PMID: 8877821

Molecular heterogeneity and glycosylation modulation of rat pituitary prolactin isoforms **synthesized and secreted in vitro in postnatal ontogeny, gestation, lactation and weaning.**

Bollengier F; Mahler A; Matton A; Vanhaelst L

Laboratorium voor Farmacologie, Faculteit Geneeskunde en Farmacie, Vrije Universiteit Brussel, Belgium.
Journal of neuroendocrinology (ENGLAND) Sep 1996, 8 (9) p721-30, ISSN 0953-8194 Journal Code: 8913461
Erratum in J Neuroendocrinol 1996 Dec;8(12) 908
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

The modulation of both the molecular size heterogeneity and the relative distribution of rat **prolactin** variants, synthesized and secreted in vitro by rat pituitary cells in the course of postnatal ontogeny and in gestation, lactation and weaning was investigated by SDS-PAGE, immunoblotting, radioimmunological techniques and O- **sialoendopeptidase** digestion. The outcome of the experiments is as follows: 1) from day 1 of postnatal life 20-, 23-, 26-, 40-44 kDa and oligomeric rat **prolactin** **isoforms** were stored and secreted; 2) perinatal life is characterized by a high degree of variability of **prolactin** size **isoforms** and their respective repartition in storage and release; in addition to the major variants, transient ones of M, 25-, 28-, 33- and 36 kDa were secreted and/or stored; 3) O- **sialoglycoprotease** digestion of pituitary cell lysate gave good evidence for 25 kDa **prolactin** being a glycoform; 4) at 1 month of age 16 kDa rat **prolactin** appeared and persisted over the whole postnatal span (1 day-->1 year) but only in stored form; 5) the physiology of gestation was essentially characterized by the M(r)-modulation of the glycoform (26 kDa-->26.3 kDa) and the virtual absence of stored 26 kDa rat **prolactin** at week 1 of pregnancy; 6) in lactation and weaning uncommon multiple banding was observed in secreted oligomeric **prolactin** ; 7) in pregnancy, lactation and weaning the differential distribution of released and stored **prolactin** **isoforms** displayed a considerable intra- and intervariability; 8) in the vast array of size **isoforms** observed in all our experiments monomeric 23 kDa **prolactin** was always the dominating variant. In conclusion, the molecular size heterogeneity and the differential distribution of secreted and stored rat pituitary **prolactin** is considerably influenced by age and physiological stimuli. The nature of polymeric **prolactin** and of the transient variants is presently unclear, and the exact physiological role of molecular heterogeneity modulation is unknown, both in humans and rat, but the patterns of change we observed in definite stages of life, suggest that this phenomenon is important in the maturation of the hypothalamus-pituitary axis and in the metabolic and hormonal changes accompanying gestation.

Tags: Animal; Female; Pregnancy; Support, Non-U.S. Gov't
Descriptors: Pituitary Gland--physiology--PH; * **Prolactin** --metabolism --ME; Glycosylation; Isomerism; Lactation--physiology--PH; Pituitary Gland --embryology--EM; Pituitary Gland--growth and development--GD; **Prolactin** --biosynthesis--BI; **Prolactin** --secretion--SE; Rats; Rats, Wistar; Weaning
CAS Registry No.: 9002-62-4 (Prolactin)
Record Date Created: 19970110
Record Date Completed: 19970110

14/9/12
DIALOG(R)File 155:MEDLINE(R)

10462449 96269272 PMID: 8778716
Isoforms **of luteinizing hormone]**
Izoformy hormonu luteinizujacego.
Szewczuk A; Kochanowska I E; Kurowska E
Laboratorium Biochemii Instytutu Immunologii i Terapii Doswiadczalnej PAN im. L. Hirszfelda we Wroclawiu.
Postepy higieny i medycyny doswiadczalnej (POLAND) 1996, 50 (1) p9-20, ISSN 0032-5449 Journal Code: 0421052
Document type: Journal Article; Review; Review, Tutorial ; English Abstract
Languages: POLISH
Main Citation Owner: NLM

Record type: Completed
Subfile: INDEX MEDICUS
Luteinizing hormone (LH) is a heterodimeric glycoprotein containing varied amount of **sialic** acid. This is a reason of numerous LH **isoforms** called also isohormones. The hormone **isoforms** were separated usually by gel electrophoresis, isoelectrofocusing or chromatofocusing. They differ in biological and immunological activity. Human and some animals LH **isoforms** were reviewed. Also some genetic mutants of LH are described. Problems of the human **isoforms** for pathology and diagnostics are presented. (54 Refs.)
Tags: Animal; Female; Human
Descriptors: **Luteinizing Hormone** --physiology--PH; Adult; Child; Genital Diseases, Female--blood--BL; Genital Diseases, Female--diagnosis--DI; Kidney Diseases--diagnosis--DI; **Luteinizing Hormone** --analysis--AN; **Luteinizing Hormone** --chemistry--CH
CAS Registry No.: 9002-67-9 (Luteinizing Hormone)
Record Date Created: 19960917
Record Date Completed: 19960917

14/9/13
DIALOG(R)File 155:MEDLINE(R)

10352361 96155123 PMID: 8563483
Thyrotropic action of human chorionic gonadotropin .
Yoshimura M; Hershman J M
Second Department of Internal Medicine, Kansai Medical University, Osaka, Japan.
Thyroid - official journal of the American Thyroid Association (UNITED STATES) Oct 1995, 5 (5) p425-34, ISSN 1050-7256 Journal Code: 9104317
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Hyperthyroidism or increased thyroid function has been reported in many patients with trophoblastic tumors. In these cases, greatly increased human chorionic **gonadotropin** (hCG) levels and suppressed TSH levels suggest that hCG has thyrotropic activity. Recent investigations have clarified the structural homology not only in the hCG and TSH molecules but also in their receptors, and this homology suggests the basis for the reactivity of hCG with the TSH receptor. The clinical significance of the thyrotropic action of hCG is now also recognized in normal pregnancy and hyperemesis gravidarum. Highly purified hLH binds to recombinant hTSH receptor and is about 10 times as potent as purified hCG in increasing cAMP. The beta-subunits of hCG and hLH share 85% sequence identity in their first 114 amino acids but differ in the carboxy-terminal peptide because hCG beta contains a 31-amino acid extension (beta-CTP). A recombinant mutant hCG that lacks beta-CTP showed almost identical potency to LH on stimulation of recombinant hTSH receptor. If intact hCG were as potent as hLH in regard to its thyrotropic activity, most pregnant women would become thyrotoxic. One of the roles of the beta-CTP may be to prevent overt hyperthyroidism in the first trimester of pregnancy when a large amount of hCG is produced by the placenta. Nicked hCG preparations, obtained from patients with trophoblastic disease or by enzymatic digestion of intact hCG, showed approximately 1.5- to 2-fold stimulation of recombinant hTSH receptor compared with intact hCG. This suggests that the thyrotropic activity of hCG may be influenced by the metabolism of the hCG molecule itself. Deglycosylation and/or desialylation of hCG enhances its thyrotropic potency. Basic hCG **isoforms** with lower **sialic** acid content extracted from hydatidiform moles were more potent in activating adenylate cyclase, and showed high bioactivity/immunoactivity (B/I) ratio in CHO cells expressing human TSH receptors. This is consistent with the finding that the beta-CTP truncated hCG with higher thyrotropic potency is substantially deglycosylated and desialylated in the beta-subunit relative to intact hCG because all four O-linked glycosylation sites occur within the missing C-terminal extension. The desialylated hCG variant also interacts directly

with recombinant hTSH receptors transfected into human thyroid cancer cells. There is thyroid-stimulating activity in sera of normal pregnant women, and this correlates with serum hCG levels. The thyroid gland of normal pregnant women may be stimulated by hCG to secrete slightly excessive quantities of T4 and induce a slight suppression of TSH, perhaps being about 1 mU/L less than nongravid levels, but not high enough to induce overt hyperthyroidism. Maternal thyroid glands may secrete more thyroid hormone during early pregnancy in response to the thyrotropic activity of hCG that overrides the normal operation of the hypothalamic-pituitary-thyroid feedback system. Biochemical hyperthyroidism associated with hyperemesis gravidarum has been attributed to hCG. In patients with hyperemesis gravidarum, thyrotropic in serum correlated with hCG immunoreactivity, and the severity of vomiting as indicated by clinical and biochemical parameters correlated with the degree of thyroid stimulation. To understand the thyrotropic action of hCG, it is necessary to know whether hCG activates the same domain of the TSH receptor as does TSH. The identification of the molecular structure of the hCG **isoform** with the highest thyrotropic potency will resolve the enigma of gestational thyrotoxicosis and the hyperthyroidism associated with trophoblastic disease and hCG-producing tumors. (62 Refs.)

Tags: Animal; Female; Human; Pregnancy; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.

Descriptors: Chorionic **Gonadotropin** --pharmacology--PD; *Thyrotropin --pharmacology--PD; Amino Acid Sequence; Chorionic **Gonadotropin** --chemistry--CH; Molecular Sequence Data; Receptors, Thyrotropin--drug effects--DE; Sequence Homology; Thyrotropin--chemistry--CH

CAS Registry No.: 0 (Chorionic Gonadotropin); 0 (Receptors, Thyrotropin); 9002-71-5 (Thyrotropin)

Record Date Created: 19960301

Record Date Completed: 19960301

14/9/14

DIALOG(R)File 155:MEDLINE(R)

10339634 96141991 PMID: 8550754

More basic isoforms **of serum** gonadotropins **during** gonadotropin **-releasing hormone agonist therapy in pubertal children.**

Wide L; Albertsson-Wikland K; Phillips D J

Department of Clinical Chemistry, University Hospital, Uppsala, Sweden.

Journal of clinical endocrinology and metabolism (UNITED STATES) Jan 1996, 81 (1) p216-21, ISSN 0021-972X Journal Code: 0375362

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

An acute challenge of exogenous GnRH elicits rapidly increased serum **gonadotropin** levels with qualitative changes to more basic **isoforms** of both FSH and LH. Chronic GnRH agonist therapy suppresses endogenous **gonadotropins**, and the serum levels of FSH and LH are low and fairly constant. A possible qualitative change in the **gonadotropins** during GnRH agonist therapy was investigated by determination of the median charge of the **gonadotropin isoforms** before and during therapy in 18 pubertal children. Two different GnRH agonists were studied: buserelin, given intranasally or as a sc implant for 1.5-34 months to five girls, aged 7-10 yr, and for 5-6 months to two boys, aged 11-13 yr; and triptorelin, administered as a depot preparation for 3-6 months to four girls, aged 9-12.5 yr, and for 1-24 months to seven boys, aged 10.5-12 yr. FSH and LH in serum and eluates after electrophoresis in 0.10% agarose suspension were measured with sandwich fluoroimmunoassays. The mean serum FSH and LH levels decreased significantly ($P < 0.05$) in girls during triptorelin therapy, whereas only the FSH level decreased ($P < 0.05$) in the boys. There were no significant ($P > 0.05$) changes in serum **gonadotropin** levels during buserelin therapy. All of the children had more basic serum **isoforms** of LH, and all but one had more basic forms of FSH during the GnRH agonist treatments. In a girl who had more basic **gonadotropin isoforms** after treatment with triptorelin for 2 and 6 months, a GnRH challenge elicited

the release of still more basic **isoforms** . The changes in mean median charge to more basic **gonadotropin isoforms** were highly significant for both busereline (P < 0.01) and triptorelin (P < 0.001) treatment. An increased (P < 0.001) degree of charge heterogeneity was observed for FSH after triptorelin therapy. These findings show that there is a qualitative change in the **isoforms** of both FSH and LH in serum during GnRH agonist therapy in pubertal children. The changes in charge to more basic **gonadotropin isoforms** most likely reflect a direct effect at the pituitary level, leading to the synthesis and/or selective release of less **sialylated** and sulfated **isoforms** of the **gonadotropins** . The observed qualitative changes in the **gonadotropin isoforms** in these pubertal children may be part of the clinical effects of GnRH agonist therapy, leading to an arrest or regression of puberty.

Tags: Female; Human; Male

Descriptors: Buserelin--therapeutic use--TU; * **Follicle Stimulating Hormone** --blood--BL; * **Luteinizing Hormone** --blood--BL; *Puberty--blood--BL ; *Triptorelin--therapeutic use--TU; Adolescent; Child

CAS Registry No.: 57773-63-4 (Triptorelin); 57982-77-1 (Buserelin); 9002-67-9 (Luteinizing Hormone); 9002-68-0 (Follicle Stimulating Hormone)

Record Date Created: 19960220

Record Date Completed: 19960220

14/9/15

DIALOG(R)File 155:MEDLINE(R)

08644045 95332639 PMID: 7608469

Application of a sensitive HPLC-based fluorometric assay to determine the sialic **acid content of human** gonadotropin isoforms .

Stanton P G; Shen Z; Kecorius E A; Burgon P G; Robertson D M; Hearn M T

Centre for Bioprocess Technology, Monash University, Victoria, Australia.

Journal of biochemical and biophysical methods (NETHERLANDS) Feb 1995, 30 (1) p37-48, ISSN 0165-022X Journal Code: 7907378

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The human pituitary **gonadotropins** , follitropin (hFSH) and lutropin (hLH) are glycoproteins which are microheterogeneous in terms of their charge and molecular size, as well as their in vitro and in vivo bioactivities. The aim of this study was to determine the contribution of variations in **sialic** acid (N-acetyl neuraminic acid) content to the structural heterogeneity of these glycoproteins. **Sialic** acid (Neu5Ac) was released by partial acid hydrolysis (0.1 M TFA, 80 degrees C, 1 h) and derivatised with the fluorescent label DMB (1,2-diamino-4,5-methylenedioxyb enzene) in conjunction with an internal standard (N-glycoyl-neuraminic acid). The derivatives were then separated by reversed-phase HPLC. This method allowed quantitation of the **sialic** acid content over a range of 5-100 pmol with between assay variation of < 6% for **sialic** acid released from approximately 100 ng (3 pmol) of hFSH or hLH. Comparison of the **sialic** acid contents of standard **sialylated** glycoproteins by either DMB-derivatisation or high-performance anion-exchange chromatography with pulsed amperometric detection yielded similar results, confirming the reliability of the fluorescence detection method. The **sialic** acid contents of 9 hFSH **isoforms** varied between 1.5-13.7 mol Neu5AC/mol FSH, whilst a range of 1.1-9.1 mol Neu5AC/mol LH was observed for 12 hLH **isoforms** . The **sialic** acid content of the hFSH **isoforms** was also observed to be related to the hormonal specific activity in a radioreceptor assay, confirming that alterations in the carbohydrate structure can influence the FSH-receptor interaction. In contrast, the **sialic** acid content of the hLH **isoforms** was found to be not related to specific activity at the receptor level.

Tags: Human; Support, Non-U.S. Gov't

Descriptors: Chromatography, High Pressure Liquid; *Fluorometry--methods --MT; * **Follicle Stimulating Hormone** --chemistry--CH; * **Luteinizing Hormone** --chemistry--CH; * **Sialic** Acids--analysis--AN; Fluorescent Dyes;

Hydrolysis; Linear Models; N-Acetylneuraminic Acid; Phenylenediamines; Reference Standards; Sensitivity and Specificity
CAS Registry No.: 0 (Fluorescent Dyes); 0 (Phenylenediamines); 0 (Sialic Acids); 131-48-6 (N-Acetylneuraminic Acid); 38608-07-0 (1,2-diamino-4,5-methylenedioxybenzene); 9002-67-9 (Luteinizing Hormone); 9002-68-0 (Follicle Stimulating Hormone)
Record Date Created: 19950817
Record Date Completed: 19950817

14/9/16
DIALOG(R)File 155:MEDLINE(R)

08575420 95263722 PMID: 7745007
Variation in the thyrotropic activity of human chorionic gonadotropin **in Chinese hamster ovary cells arises from differential expression of the human thyrotropin receptor and microheterogeneity of the hormone.**
Hoermann R; Poertl S; Liss I; Amir S M; Mann K
Department of Medicine, University of Essen, Germany.
Journal of clinical endocrinology and metabolism (UNITED STATES) May 1995, 80 (5) p1605-10, ISSN 0021-972X Journal Code: 0375362
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIM; INDEX MEDICUS
The role of hCG as a stimulator of the human thyroid has been a subject of controversy, because discrepant results have been obtained in different in vitro assays. In an attempt to explain the variation observed in the thyroid response to hCG, we investigated the ability of hCG and that of its **isoforms** and glycosylation variants to inhibit [125I]bovine (b) TSH binding and stimulate adenylate cyclase in two clones, JP09 and JP26, of Chinese hamster ovary cells stably transfected with the human TSH receptor (hTSHr). The two clones differed with respect to the number of hTSHr expressed per cell (34,000 in JP09 and 2,000 in JP26 cells). Both responded extremely well to bTSH; the cAMP response to 0.001 IU/L bTSH was distinguishable from basal values. Interestingly, JP09 cells were readily stimulated by hCG (20-100 mg/L; 0.52-2.6 x 10(-6) mol/L) to release cAMP, whereas JP26 cells showed little if any response. Also, cAMP stimulation produced by asialo-hCG was 12-fold in JP09 cells and only 4-fold in JP26 cells compared to 45- and 67-fold stimulations by bTSH, respectively. Stimulation by asialo-hCG was approximately 30% that of bTSH in JP09 cells, but less than 6% in JP26 cells. When assessing the thyrotropic activity of the microheterogeneous **isoforms** of hCG, more alkaline pI forms were found to be more active than those of a more acidic pI regardless of whether they were derived from normal or molar pregnancy urine. Further studies with hCG, asialo-hCG, asialoagalacto-hCG, and deglycosylated hCG revealed that removal of **sialic** acid caused a marked increase in both its affinity for hTSHr and its cAMP-releasing potency, whereas removal of further carbohydrate, although it slightly enhanced receptor binding, was detrimental to adenylate cyclase activation. In conclusion, differences in hTSHr expression may cause a variation in the cAMP response to hCG or its glycosylation variants, as does the microheterogeneity of the hormone itself. These mechanisms may be responsible at least in part for the divergent responses of different cell types to hCG and render interpretation of the physiological meaning of the data obtained in recombinant receptor systems difficult.
Tags: Animal; Human; Support, Non-U.S. Gov't
Descriptors: CHO Cells--metabolism--ME; *Chorionic **Gonadotropin** --pharmacology--PD; *Receptors, Thyrotropin--metabolism--ME; *Thyrotropin --metabolism--ME; Asialoglycoproteins--pharmacology--PD; Chorionic **Gonadotropin** --chemistry--CH; Cyclic AMP--metabolism--ME; Hamsters; Infant, Newborn; Isomerism; Thyrotropin--antagonists and inhibitors--AI
CAS Registry No.: 0 (Asialoglycoproteins); 0 (Chorionic Gonadotropin); 0 (Receptors, Thyrotropin); 0 (asialo-human chorionic gonadotropin); 60-92-4 (Cyclic AMP); 9002-71-5 (Thyrotropin)
Record Date Created: 19950615
Record Date Completed: 19950615

14/9/17
DIALOG(R)File 155:MEDLINE(R)

08512464 95200740 PMID: 7765934
Role of environmental conditions on the expression levels, glycoform pattern and levels of sialyltransferase **for hFSH produced by recombinant CHO cells.**
Chotigeat W; Watanapokasin Y; Mahler S; Gray P P
Department of Biotechnology, University of New South Wales, Sydney, Australia.
Cytotechnology (NETHERLANDS) 1994, 15 (1-3) p217-21, ISSN 0920-9069 Journal Code: 8807027
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: BIOTECHNOLOGY
A recombinant CHO cell line in which the expression of human follicle stimulating hormone (hFSH) was under the control of the beta actin promoter was maintained in steady state perfusion cultures on a protein free medium. The level of expression of the hFSH was controlled by varying the steady state level of dissolved oxygen (10-90% of air saturation) and of sodium butyrate (0-1.5mM). Under these conditions, the specific productivity of hFSH (qFSH) varied from 0.7 to 4.8 ng hFSH/10(6) cells/h. As the specific productivity of hFSH increased, there was a shift in the FSH **isoforms** to the lower pI fractions, corresponding to increased **sialic** acid content. As the specific productivity of hFSH increased, shifting the **isoform** distribution towards the lower pI **isoforms** , that the **sialyltransferase** enzymic activity also increased.
Tags: Animal; Human; Support, Non-U.S. Gov't
Descriptors: **Follicle Stimulating Hormone** --biosynthesis--BI; *Recombinant Proteins--biosynthesis--BI; * **Sialyltransferases** --metabolism --ME; *Tissue Culture--methods--MT; Actins--genetics--GE; Biotechnology --instrumentation--IS; Biotechnology--methods--MT; Butyric Acid; Butyric Acids--pharmacology--PD; CHO Cells; Gene Expression; Glycosylation; Hamsters; Kinetics; Oxygen--pharmacology--PD; Promoter Regions (Genetics); **Sialic** Acids--metabolism--ME; Time Factors
CAS Registry No.: 0 (Actins); 0 (Butyric Acids); 0 (Recombinant Proteins); 0 (Sialic Acids); 107-92-6 (Butyric Acid); 7782-44-7 (Oxygen); 9002-68-0 (Follicle Stimulating Hormone)
Enzyme No.: EC 2.4.99.- (**Sialyltransferases**)
Record Date Created: 19950425
Record Date Completed: 19950425

14/9/18
DIALOG(R)File 155:MEDLINE(R)

08291837 94358076 PMID: 8077357
Increased biological activity due to basic isoforms **in recombinant human follicle-stimulating hormone produced in a human cell line.**
Flack M R; Bennet A P; Froehlich J; Anasti J N; Nisula B C
Developmental Endocrinology Branch, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland 20892.
Journal of clinical endocrinology and metabolism (UNITED STATES) Sep 1994, 79 (3) p756-60, ISSN 0021-972X Journal Code: 0375362
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIM; INDEX MEDICUS
FSH has four asparagine-linked oligosaccharides with variable **sialic** acid contents, so that FSH is not a single molecule, but a heterogeneous group of **isoforms** . These **isoforms** differ in their biological properties

and their distribution changes in various physiological states, allowing the modulation of FSH activity. Recombinant human (h) FSH has been produced in Chinese hamster ovary cells and has an **isoform** profile similar to those of both pituitary FSH standard and purified urinary FSH. These FSH preparations, however, do not contain the full spectrum of FSH **isoforms** found in the circulation. Production of recombinant hFSH in a cell line with a different pattern of glycosylation could broaden its **isoform** profile and potentially alter its biological activity. Thus, we transfected human embryonal kidney cells (293) with the human alpha and FSH beta genes to produce recombinant hFSH (hFSH-293) and determined its biological activity in a rat granulosa cell bioassay. Although hFSH-293 was immunologically indistinguishable from pituitary FSH standard, its biological potency was 3- to 6-fold higher than those of two different pituitary FSH standards. To investigate this increased potency, we separated the **isoforms** of hFSH-293 by chromatofocusing and determined their biological potencies in the rat granulosa cell bioassay. The **isoform** profile of hFSH-293 demonstrated a greater number of basic **isoforms** than that of pituitary FSH standard. Several of these basic **isoforms** exhibited enhanced in vitro biological potency, accounting for the increased biological potency of hFSH-293. This pattern of high in vitro biological activity and more basic **isoforms** is analogous to the FSH circulating during GnRH stimulation, pubertal induction, and ovulation.

Tags: Animal; Female; Human

Descriptors: **Follicle Stimulating Hormone** --chemistry--CH; * **Follicle Stimulating Hormone** --pharmacology--PD; Cell Line; Chromatography; Embryo; Estradiol--biosynthesis--BI; **Follicle Stimulating Hormone** --genetics--GE; Glycosylation; Granulosa Cells--drug effects--DE; Granulosa Cells --metabolism--ME; Hydrogen-Ion Concentration; Immunoassay; Kidney; Rats; Recombinant Proteins--metabolism--ME; Transfection

CAS Registry No.: 0 (Recombinant Proteins); 50-28-2 (Estradiol); 9002-68-0 (Follicle Stimulating Hormone)

Record Date Created: 19941006

Record Date Completed: 19941006

14/9/19

DIALOG(R)File 155:MEDLINE(R)

08143503 94209372 PMID: 8157712

Thyrotropic activity of basic isoelectric forms of human chorionic gonadotropin **extracted from hydatidiform mole tissues.**

Yoshimura M; Pekary A E; Pang X P; Berg L; Goodwin T M; Hershman J M

Endocrinology Research Laboratory, West Los Angeles Veterans Affairs Medical Center, California 90073.

Journal of clinical endocrinology and metabolism (UNITED STATES) Apr 1994, 78 (4) p862-6, ISSN 0021-972X Journal Code: 0375362

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

hCG is known to have thyroid-stimulating activity and may cause hyperthyroidism in patients with trophoblastic diseases. hCG occurs in normal and molar pregnancy with breaks or nicks in the alpha- or beta-subunit peptide linkage and with substantial heterogeneity in the composition and degree of branching within the oligosaccharide side-chains. The bioactivity of hCG is markedly influenced by these structural variations. We purified hCG from five hydatidiform moles, using chromatofocusing separation after gel filtration. The hCG molecules were fractionated according to their isoelectric points, with a linear pH gradient from 3.2-6.1 and a final 1.0 mol/L NaCl step elution. The hCG immunoreactivity of each fraction was measured by RIA, and the thyroid-stimulating activity of hCG was determined by means of the cAMP response in Chinese hamster ovary cells expressing functional human TSH receptors (Chinese hamster ovary-JP09 cells). The chromatofocusing profile showed that hCG from the moles was eluted in six or seven major peaks at pH 6.1, 5.5, 5.3, 4.8, 3.8, and 3.2 and with 1.0 mol/L NaCl, whereas hCG extracted from serum of hydatidiform moles and standard hCG preparation

CR-127 extracted from pregnancy urine showed only small peaks at pH greater than 5.3. Each fraction increased cAMP production significantly in Chinese hamster ovary-JP09 cells. The relative bioactivity/immunoreactivity, represented as the ratio of cAMP/hCG (picomoles per IU), was significantly higher in basic components (pI 6.1, 6.2 +/- 1.2; pI 5.5, 4.4 +/- 2.7; pI 5.3, 5.8 +/- 0.3) than in hCG CR-127 (bioactivity/immunoreactivity, 0.42; P < 0.05). The difference in pI of each hCG **isoform** was attributable to the extent of **sialylation** ; basic hCG **isoforms** contained less **sialic** acid by immunological detection using lectins. These results indicate that **isoforms** of hCG with more thyrotropic activity were produced by trophoblastic tissues in patients with hydatidiform mole. We speculate that these **isoforms** of hCG may be responsible for the hyperthyroidism in some patients with hydatidiform moles.

Tags: Animal; Female; Human; Pregnancy; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.

Descriptors: Chorionic **Gonadotropin** --analysis--AN; *Chorionic **Gonadotropin** --physiology--PH; *Hydatidiform Mole--chemistry--CH; *Thyroid Gland--physiology--PH; *Uterine Neoplasms--chemistry--CH; Adult; CHO Cells; Chorionic **Gonadotropin** --blood--BL; Cyclic AMP--metabolism--ME; Hamsters; Hydatidiform Mole--pathology--PA; Hydrogen-Ion Concentration; Isoelectric Focusing; Isomerism; Radioimmunoassay; Receptors, Thyrotropin--analysis--AN ; Receptors, Thyrotropin--physiology--PH; Thyroid Gland--chemistry--CH; Thyroid Gland--ultrastructure--UL; Uterine Neoplasms--pathology--PA

CAS Registry No.: 0 (Chorionic Gonadotropin); 0 (Receptors, Thyrotropin); 60-92-4 (Cyclic AMP)

Record Date Created: 19940519

Record Date Completed: 19940519

14/9/20

DIALOG(R)File 155:MEDLINE(R)

07736119 93191397 PMID: 1294011

[Glycoprotein hormones, glycosylation and biological activity]

Hormones glycoproteiques, glycosylation et activite biologique.

Pigny P; Berault A; Dewailly D; Boersma A

Laboratoire d'endocrinologie, USN A, CHU Lille, France.

Annales de biologie clinique (FRANCE) 1992, 50 (8) p557-64, ISSN 0003-3898 Journal Code: 2984690R

Document type: Journal Article; Review; Review, Tutorial ; English Abstract

Languages: FRENCH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Glycoprotein hormones LH, FSH, TSH and hCG are heterodimeric molecules: each contains two subunits, a common alpha and a unique beta subunit. Each subunit bears one or two Asparagine linked carbohydrate moieties which have a biantennary complex-type or hybrid-type structure. Different technical methods as deglycosylation or molecular biology techniques have been used to study the role of carbohydrate residues in hormonal bioactivity. The carbohydrate chains are not directly involved in receptor binding events but their mechanisms of action is not fully understood. Two hypotheses are frequently emphasised: a conformational role or an involvement in the coupling of the receptor-adenylate cyclase system. At the post receptor level carbohydrate chains modulate the bioactivity in two ways: a global regulation following an all-or-none mode and slight one. The removal of the carbohydrate moieties leads to a loss of the in vitro hormonal activity. The results observed are dependent of the deglycosylation techniques and the bioactivity tests used. Hormone's deglycosylation reduces their capacity of production of cAMP and, to a lesser extent, their steroidogenic power. Deglycosylated hormones are antagonists to negative hormones although deglycosylated hCG has some agonist properties in vivo. Microheterogeneity of the glycoprotein hormones is due to slight variations in **sialic** acid and/or sulfate content. Glycoprotein hormones exist as several **isoforms** which differ in biological potency. Alkaline **isoforms** (less **sialylated** ones) are the most biologically active in vitro but have a short half live in vivo; acid **isoforms** are less active in vitro

but have a longer circulatory half live. The polymorphism of glycoprotein hormones is a highly regulated process.(ABSTRACT TRUNCATED AT 250 WORDS) (74 Refs.)
Tags: In Vitro
Descriptors: Chorionic **Gonadotropin** --metabolism--ME; * **Follicle Stimulating Hormone** --metabolism--ME; * **Luteinizing Hormone** --metabolism --ME; *Thyrotropin--metabolism--ME; Glycosylation; Polysaccharides --metabolism--ME; Receptors, FSH--metabolism--ME; **Receptors, Gonadotropin --metabolism** --ME; Receptors, LH--metabolism--ME; Receptors, Thyrotropin --metabolism--ME
CAS Registry No.: 0 (Chorionic Gonadotropin); 0 (Polysaccharides); 0 (Receptors, FSH); 0 (Receptors, Gonadotropin); 0 (Receptors, LH); 0 (Receptors, Thyrotropin); 9002-67-9 (Luteinizing Hormone); 9002-68-0 (Follicle Stimulating Hormone); 9002-71-5 (Thyrotropin)
Record Date Created: 19930407
Record Date Completed: 19930407

14/9/21
DIALOG(R)File 155:MEDLINE(R)

07497280 92360983 PMID: 1498420
Subunit-specific sulphation of oligosaccharides relating to charge-heterogeneity in porcine lutrophin isoforms .
Ujihara M; Yamamoto K; Nomura K; Toyoshima S; Demura H; Nakamura Y; Ohmura K; Osawa T
Department of Medicine, Tokyo Women's Medical College, Japan.
Glycobiology (ENGLAND) Jun 1992, 2 (3) p225-31, ISSN 0959-6658 Journal Code: 9104124
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Lutrophin (LH) consists of an array of **isoforms** with different charges and bioactivities. This study was undertaken to clarify specifically how oligosaccharides of alpha and beta subunits contribute to LH **isoform** charges. Porcine LH (pLH) was separated into four **isoforms** by isoelectric focusing (IEF), followed by subunit isolation. Their oligosaccharides were released by hydrazinolysis, labelled by reduction with NaB3H4, and fractionated by HPLC with a Mono Q column into five populations differing in the number of sulphate (S) and **sialic** acid (N) residues, designated as Neutral, N-1, S-1, S-N and S-2. Oligosaccharides were predominantly sulphated (S-1 and S-2) and infrequently **sialylated** (N-1 and S-N). Further analysis, including concanavalin A (Con A) affinity chromatography, desialylation, desulphation, sequential exoglycosidase digestion and methylation, clarified the structures of the acidic oligosaccharides. All were of the biantennary complex type. Their two peripheral branches were SO4-4GalNAc beta 1-4Glc-NAc and GalNAc beta 1-4GlcNAc or GlcNAc in S-1, SO4-4GalNAc beta 1-4GlcNAc and Sia alpha 2-6Gal beta 1-4GlcNAc in S-N, and (SO4-4GalNAc beta 1-4GlcNAc)2 in S-2 (where GalNAc is N-acetylgalactosamine and GlcNAc is N-acetylglucosamine). Ten percent of S-1 and of S-N had a bisecting GlcNAc residue. Sulphate residues occurred in nearly the same amount for both subunits; however, the alpha and beta subunits were sulphated differently. S-1 predominated in the alpha subunit, while S-1 and S-2 were major components in the beta subunit.(ABSTRACT TRUNCATED AT 250 WORDS)
Tags: Animal; Support, Non-U.S. Gov't
Descriptors: **Luteinizing Hormone** --chemistry--CH; *Oligosaccharides --chemistry--CH; Carbohydrate Conformation; Carbohydrate Sequence; Chromatography, Affinity; Chromatography, Ion Exchange; Electrochemistry; Methylation; Molecular Sequence Data; Molecular Structure; Oligosaccharides --isolation and purification--IP; Sulfates--chemistry--CH; Swine
CAS Registry No.: 0 (Oligosaccharides); 0 (Sulfates); 9002-67-9 (Luteinizing Hormone)
Record Date Created: 19920915
Record Date Completed: 19920915

14/9/22
DIALOG(R)File 155:MEDLINE(R)

07314234 92177208 PMID: 1795252
Comparison of the microheterogeneity of horse LH and FSH in the pituitary with that secreted into pituitary venous blood at oestrus.
Shand N; Alexander S L; Irvine C H
Department of Animal & Veterinary Sciences, Lincoln University, Canterbury, New Zealand.
Journal of reproduction and fertility. Supplement (ENGLAND) 1991, 44 p1-11, ISSN 0449-3087 Journal Code: 0225652
Contract/Grant No.: DK38322; DK; NIDDK
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
For aqueous extracts of pituitary glands of oestrous mares, luteinizing hormone (LH) profiles were found to be similar to each other and to earlier work after chromatofocussing (CF) and isoelectricfocussing (IEF). After CF, both LH and follicle-stimulating hormone (FSH) in pituitary extracts focussed in multiple peaks in the acidic range, with 86% of LH and 80% of FSH found between pH 4 and 6. By contrast, in pituitary venous plasma, only 18% of the LH focussed in this range, whereas a significantly greater proportion (P less than 0.01) eluted above pH 7 than occurred in pituitary extracts (37% vs 2%, respectively). For pituitary venous FSH, there was only a slight shift in the distribution of **isoforms** compared with the pituitary extract, with a rise in the percentage of strongly acidic molecules in pituitary venous plasma (pH less than 3.65; 34% vs 16%). These results show that at oestrus, horse LH (which differs from that of other species because it has a heavily **sialylated** C-terminal extension to the beta-subunit, as does eCG), is much more alkaline when secreted as opposed to when it is stored in the pituitary. The authors of this report suggest that this modification is made after entry into a preferentially released pool of LH. Modulation of the forms of LH and FSH that are secreted may play a role in regulating target tissue responses.
Tags: Animal; Comparative Study; Female; Support, U.S. Gov't, P.H.S.
Descriptors: Estrus--physiology--PH; * **Follicle Stimulating Hormone** --metabolism--ME; * **Gonadotropins** , Equine--metabolism--ME; *Horses --physiology--PH; * **Luteinizing Hormone** --metabolism--ME; *Pituitary Gland --physiology--PH; **Follicle Stimulating Hormone** --blood--BL; Isoelectric Point; **Luteinizing Hormone** --blood--BL
CAS Registry No.: 0 (Gonadotropins, Equine); 9002-67-9 (Luteinizing Hormone); 9002-68-0 (Follicle Stimulating Hormone)
Record Date Created: 19920407
Record Date Completed: 19920407

14/9/23
DIALOG(R)File 155:MEDLINE(R)

06624810 90250373 PMID: 2187048
Gonadotrophin **glycosylation and function.**
Wilson C A; Leigh A J; Chapman A J
Department of Obstetrics and Gynaecology, St George's Hospital Medical School, London.
Journal of endocrinology (ENGLAND) Apr 1990, 125 (1) p3-14, ISSN 0022-0795 Journal Code: 0375363
Document type: Journal Article; Review; Review, Academic
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
This review emphasizes the heterogeneous structure of the **gonadotrophin** hormones and the influence of different oligosaccharide structures on the bioactivity of these hormones. A summary has been made of the changes in

biopotency of the **gonadotrophins** throughout the life-cycle of the human and in different endocrine states in the rat. In general it appears that the charge of the **gonadotrophin** conferred by the acid radicals attached to the terminal groups on the oligosaccharide structures strongly influences biopotency. Basic structures have a greater potency in in-vitro assays, but a short half-life in the circulation, while acidic **isoforms** are less potent, but have a longer circulatory time and are thus more active in in-vivo estimations. More basic forms are secreted over the adult reproductive years compared with the prepubertal period and old age. The glycosyl structure of the carbohydrate groups also alters in different endocrine states and is probably also important for the bioactivity and potency of the hormone. **Gonadotrophin** -releasing hormone (GnRH) and gonadal steroids can influence the type of **isoform** synthesized and released, and therefore affect the function of **gonadotrophins** . GnRH enhances glycosylation, sulphation and biopotency. Oestradiol potentiates the glycosylation induced by GnRH and reduces **sialylation** , while testosterone increases **sialylation** . (122 Refs.)

Tags: Animal; Female; Human; Male; Support, Non-U.S. Gov't

Descriptors: **Gonadotropins** --physiology--PH; Adolescent; Adult; Glycosylation; Infant, Newborn; Middle Age; Oligosaccharides--metabolism --ME; Pituitary Hormone-Releasing Hormones--physiology--PH; Rats

CAS Registry No.: 0 (Gonadotropins); 0 (Oligosaccharides); 0 (Pituitary Hormone-Releasing Hormones)

Record Date Created: 19900618

Record Date Completed: 19900618

14/9/24

DIALOG(R)File 155:MEDLINE(R)

05929117 88283534 PMID: 2456202

Renotropic activity in ovine luteinizing hormone isoform **(s).**

Nomura K; Tsunasawa S; Ohmura K; Sakiyama F; Shizume K

Department of Medicine, Tokyo Women's Medical College, Japan.

Endocrinology (UNITED STATES) Aug 1988, 123 (2) p700-12, ISSN 0013-7227 Journal Code: 0375040

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

Renotropic activity was previously demonstrated in an ovine LH preparation. This preparation was further purified with a series of chromatographic steps, and the fractions were assayed for renotropic activity in vivo by their ability to stimulate [3H]thymidine incorporation into renal DNA of castrated hypophysectomized male rats. A purified preparation could be dissociated by acid treatment into two major constituent subunits, designated alpha and beta, each of which was composed of three microheterogeneous components (subunits alpha 1-3 and beta 1-3) by reverse-phase HPLC. Peptide mapping, including amino acid analyses and partial sequencing of the purified peptides, showed that 1) subunits alpha 3 and beta 3 possess the full length of the polypeptide chains, with the same amino acid sequences as those of the corresponding LH subunits alpha and beta, respectively; and 2) subunits alpha 1 and alpha 2 are complexes of three polypeptides which are missing several N-terminal residues from subunit alpha 3. Conversely, subunits beta 1 and beta 2 lack the C-terminal two residues and one residue, respectively, of subunit beta 3. Renotropic activity was not detected in any of the dissociated subunits alone, but association of alpha 1-3 with beta 1-3 reconstituted the hormonal activity with different potencies. In particular, combination of subunits alpha 3 and beta 3 (alpha 3.beta 3) yielded a potent renotropic activity with weak **gonadotropic** activity. The carbohydrate composition of the purified preparation exhibiting renotropic activity differed from that of a reference oLH preparation, which possessed greater **gonadotropic** activity but was devoid of renotropic activity. Furthermore, renotropic activity was decreased after removal of **sialic** acid by treatment with neuraminidase. Thus, the oligosaccharide moieties as well as the amino acid sequences of the subunits may play an important role in the expression of renotropic

activity in vivo, these effects over and above those arising from differential metabolic clearance. We conclude that pituitary renotropin represents a novel activity of a LH- **isoform** (s) and that the posttranslational (or the artificial, i.e. during preparation) modification of the constituent LH subunits may be responsible for modulation of renotropic activity as well as the intrinsic **gonadotropic** activity.

Tags: Animal; Male; Support, Non-U.S. Gov't

Descriptors: DNA--biosynthesis--BI; *Kidney--metabolism--ME; * **Luteinizing Hormone** --pharmacology--PD; Amino Acid Sequence; Amino Acids --analysis--AN; Carbohydrates--analysis--AN; Chromatography; Chromatography , High Pressure Liquid; Electrophoresis, Polyacrylamide Gel; **Glycoprotein Hormones, alpha Subunit** ; Hydrogen-Ion Concentration; Kidney--drug effects --DE; **Luteinizing Hormone** --isolation and purification--IP; Molecular Sequence Data; Molecular Weight; Neuraminidase--metabolism--ME; Peptide Fragments; **Pituitary Hormones, Anterior** --isolation and purification--IP; **Pituitary Hormones, Anterior** --pharmacology--PD; Radioimmunoassay; Rats; Rats, Inbred Strains; Trypsin

CAS Registry No.: 0 (Amino Acids); 0 (Carbohydrates); 0 (Glycoprotein Hormones, alpha Subunit); 0 (Peptide Fragments); 0 (Pituitary Hormones, Anterior); 9002-67-9 (Luteinizing Hormone); 9007-49-2 (DNA)

Enzyme No.: EC 3.2.1.18 (Neuraminidase); EC 3.4.21.4 (Trypsin)

Record Date Created: 19880829

Record Date Completed: 19880829

14/9/25

DIALOG(R)File 155:MEDLINE(R)

05187147 86188076 PMID: 3008870

Isolation and characterization of three forms of luteinizing hormone from the pituitary gland of the horse.

Matteri R L; Papkoff H; Ng D A; Swedlow J R; Chang Y S

Biology of reproduction (UNITED STATES) Apr 1986, 34 (3) p571-8, ISSN 0006-3363 Journal Code: 0207224

Contract/Grant No.: HD-05722; HD; NICHD

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Three **isoforms** of equine luteinizing hormone (eLH-A, eLH-B and eLH-C) have been isolated from horse pituitary glands. Separation was achieved on the basis of charge heterogeneity by ion-exchange chromatography. These charge differences were apparent after final purification, as determined by electrophoretic mobility on polyacrylamide disc gels (RF = 0.14, 0.19 and 0.26 for eLH-A, -B and -C, respectively). Apparent size differences were also noted between the isohormones by gel filtration on Sephadex G-100. Ve/Vo ratios for eLH-A, -B and -C were 1.72, 1.54 and 1.47, respectively. All 3 **isoforms** were found to contain an equivalent amount of hexose (9.0-9.2%). Isohormones eLH-B and eLH-C, however, possess more **sialic** acid than eLH-A (6.6-6.7%, vs. 4.5%). The eLH-A and eLH-B preparations contain a similar amount of hexosamine, which is slightly lower than the amount of eLH-C (8.8-9.1% vs. 11.2%). No differences were noted between the isohormones by rat Leydig cell LH bioassay, equine testis LH radioreceptor assay (RRA) or calf testis follicle-stimulating hormone (FSH) RRA. Slight, but nonsignificant, variations were noted between preparations in an eLH radioimmunoassay (RIA). Although chemical variations were detected between the eLH **isoforms** , no significant differences were observed in in vitro biological and immunological activities. The differences detected in **sialic** acid content raises the possibility that differences in in vivo clearance rates may exist.

Tags: Animal; Support, U.S. Gov't, P.H.S.

Descriptors: Horses--physiology--PH; * **Luteinizing Hormone** --isolation and purification--IP; Biological Assay; Carbohydrates--analysis--AN; Chromatography, DEAE-Cellulose; Electrophoresis, Polyacrylamide Gel; **Luteinizing Hormone** --immunology--IM; **Luteinizing Hormone** --metabolism --ME; Receptors, Cell Surface--metabolism--ME; Receptors, FSH; Receptors,

LH; Structure-Activity Relationship
CAS Registry No.: 0 (Carbohydrates); 0 (Receptors, Cell Surface); 0 (Receptors, FSH); 0 (Receptors, LH); 9002-67-9 (Luteinizing Hormone)
Record Date Created: 19860603
Record Date Completed: 19860603

14/9/26
DIALOG(R)File 155:MEDLINE(R)

05159239 86160038 PMID: 3955145
An in vitro study of LH release, synthesis and heterogeneity in pituitaries from proestrous and short-term ovariectomized rats.
Baldwin D M; Highsmith R F; Ramey J W; Krummen L A
Biology of reproduction (UNITED STATES) Mar 1986, 34 (2) p304-15, ISSN 0006-3363 Journal Code: 0207224
Contract/Grant No.: HD-16994; HD; NICHD
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
It is known that acute ovariectomy (OVX) greatly attenuates the pituitary luteinizing hormone (LH) response to **gonadotropin** -releasing hormone (GnRH) in vitro. The present study evaluated possible quantitative and/or qualitative differences in the biosynthesis and secretion of LH in pituitaries from proestrous and acutely (72 h) OVX rats. Paired anterior pituitary glands were incubated for 4 h in a medium containing +/- 10 nM GnRH. Pituitary and secreted LH were measured by radioimmunoassay with differences in total LH (tissue plus medium) +/- GnRH being indicative of GnRH-stimulated LH synthesis. Qualitative changes in LH were evaluated by isoelectrofocusing (IEF). The results show that the major form of LH stored in and released from the pituitaries consisted of LH molecules with an isoelectric point (pI) in the alkaline pH range (alkaline LH), and a lesser amount (approximately 30%) of LH molecules in the acidic pH range (acidic LH). The ratio of alkaline/acidic LH observed in the pituitary and medium was similar in the proestrous and OVX groups, although the amount of alkaline and acidic LH release in response to GnRH was 2-3 times greater in the proestrous group. In both groups, the alkaline/acidic LH ratio of secreted LH was higher in the presence of GnRH than in its absence. Alkaline LH synthesis was increased by GnRH in both groups, with the response being greater in the proestrous than in the OVX group; GnRH-stimulated acidic LH synthesis was observed only in the proestrous group. In both groups, the amount of LH synthesized was about 60% of the amount released, which suggests that LH synthesis does not fully account for differences in GnRH-stimulated LH release. Treatment of pituitary extracts with neuraminidase decreased acidic LH, and proportionately increased alkaline LH. These results suggest that the quality of LH stored in and secreted from pituitaries of proestrous and OVX rats is similar, and that there is a preferential release of the major alkaline LH **isoform** in response to GnRH. The ovarian steroid environment, presumably estradiol, proportionately increases the amount of alkaline and acidic LH released, and differentially affects the amounts of the various **isoforms** synthesized in response to GnRH. The charge heterogeneity of alkaline and acidic LH may be related to the **sialic** acid content of the LH molecule.
Tags: Animal; Female; Support, U.S. Gov't, P.H.S.
Descriptors: **Luteinizing Hormone** --metabolism--ME; *Pituitary Gland, Anterior--metabolism--ME; Isoelectric Point; **Luteinizing Hormone** --secretion--SE; Ovariectomy; Pituitary Gland, Anterior--secretion--SE; Proestrus; Rats; Time Factors
CAS Registry No.: 9002-67-9 (Luteinizing Hormone)
Record Date Created: 19860505
Record Date Completed: 19860505

14/9/27
DIALOG(R)File 155:MEDLINE(R)

04054410 83183615 PMID: 6840529

Pituitary gonadotropic **hormone from a chondrostean fish, starred sturgeon (Acipenser stellatus Pall.) III. Polymorphism.**

Kuznetzov A A; Goncharov B F; Burzawa-Gerard E

General and comparative endocrinology (UNITED STATES) Mar 1983, 49 (3) p364-74, ISSN 0016-6480 Journal Code: 0370735

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Four biologically active fractions of **gonadotropic** hormone (aci-GTH-A, -B, -C, -D) were isolated and purified from acetonized pituitaries of the starred sturgeon (Acipenser stellatus Pall.). Their separation was achieved by DEAE-cellulose chromatography. Disc-electrophoresis and especially isoelectric focusing in polyacrylamide gel showed that each fraction contained several components. Not less than 15 different components as a whole with isoelectric points ranging from 4.5 to 7.0 could be counted in four aci-GTH preparations. All these components were active in toad oocyte maturation test. Only two of four preparations (aci-GTH-A and -D) were practically free of common components. All aci-GTH preparations were shown to be homogeneous and identical by molecular weight, sedimentation coefficient, **sialic** acid content, and some immunological properties. N-terminal amino acid analysis revealed tyrosine and leucine in all aci-GTH preparations, with the only exception of aci-GTH-D that contained an additional polypeptide with N-terminal glycine. No differences in the spectra of aci-GTH **isoforms** were found when pituitary extract, newly purified or 3 years older hormone preparations were submitted to isoelectric focusing.

Tags: Animal; Comparative Study; Female; Male

Descriptors: Fishes--metabolism--ME; * **Gonadotropins** , Pituitary --isolation and purification--IP; *Pituitary Gland--analysis--AN; Biological Assay; Bufonidae; Chromatography, DEAE-Cellulose; Chromatography, Gel; Electrophoresis, Polyacrylamide Gel; **Gonadotropins** , Pituitary--pharmacology--PD; Isoelectric Focusing; Oocytes--drug effects --DE; Oocytes--growth and development--GD; Polymorphism (Genetics)

CAS Registry No.: 0 (Gonadotropins, Pituitary)

Record Date Created: 19830610

Record Date Completed: 19830610

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04jun03 16:32:39 User228206 Session D1981.3

$3.24 1.012 DialUnits File155

$5.67 27 Type(s) in Format 9

$5.67 27 Types

$8.91 Estimated cost File155

$0.22 TELNET

$9.13 Estimated cost this search

$9.13 Estimated total session cost 1.012 DialUnits

Status: Signed Off. (1 minutes)

Status: Path 1 of [Dialog Information Services via Modem]

Status: Initializing TCP/IP using (UseTelnetProto 1 ServiceID pto-dialog)
Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
******** HHHHHHHH SSSSSSSS?
Status: Signing onto Dialog
****
ENTER PASSWORD:
******** HHHHHHHH SSSSSSSS? ********
Welcome to DIALOG
Status: Connected

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Dialog level 02.14.01D

Reconnected in file 155 04jun03 16:45:19
* * * * See HELP NEWS 225 for information on new search prefixes
and display codes

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File 155:MEDLINE(R)  1966-2003/Jun W1
       (c) format only 2003 The Dialog Corp.
*File 155: Medline has been reloaded and accession numbers have
changed.  Please see HELP NEWS 155.

      Set  Items  Description
      ---  -----  -----------
Cost is in DialUnits
?s menopaus?
    S15   26323  MENOPAUS?
?s review or tutor?
          310364  REVIEW
            2239  TUTOR?
     S16  312426  REVIEW OR TUTOR?
?ds

Set     Items   Description
S1      54849   GONADOTROP?
S2      26212   R1-R2
S3      87343   R1-R18
S4     110136   (S1 OR S2 OR S3)
S5        733   S4 AND ISOFORM?
S6        310   S5 AND (DISTING? OR DIFFERENTI? OR IDENTIF? OR SEPARA? OR -
              MENOPAUS?)
S7        109   S6 AND (ASSAY? OR IMMUNOASSAY? OR EIA OR ELISA OR ELIZA OR
              METHOD?)
S8         34   S7/2000:2003
S9         75   S7 NOT S8
S10        11   S9 AND (HYBRIDOM? OR MONOCLONAL?)
S11       263   S5/2000:2003
S12       470   S5 NOT S11
S13        27   S12 AND SIAL?
S14        27   S13 NOT S10
S15     26323   MENOPAUS?
S16    312426   REVIEW OR TUTOR?
?s s15 and s16
          26323  S15
         312426  S16
     S17    1089  S15 AND S16
?s s17 and (gonad? or fsh? or lh?)
          1089  S17
         82350  GONAD?
         20439  FSH?
         40307  LH?
     S18     118  S17 AND (GONAD? OR FSH? OR LH?)
?s s18 and human?
           118  S18
       8070462  HUMAN?
     S19     114  S18 AND HUMAN?
?s s19 and (determin? or measur? or disting? or different? or analyz?)
           114  S19
       1206201  DETERMIN?
       1101594  MEASUR?
         91320  DISTING?
       1478510  DIFFERENT?
        318371  ANALYZ?
     S20      52  S19 AND (DETERMIN? OR MEASUR? OR DISTING? OR DIFFERENT?
                  OR ANALYZ?)
?s s20 and isoform?
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         46261  ISOFORM?
     S21     0  S20 AND ISOFORM?
?s s17 and predict?
          1089  S17
        340218  PREDICT?
     S22    53  S17 AND PREDICT?
?s s22 and monoclonal?
            53  S22
        167922  MONOCLONAL?
     S23     0  S22 AND MONOCLONAL?
?s s17 and monoclonal?
          1089  S17
        167922  MONOCLONAL?
     S24     6  S17 AND MONOCLONAL?
?t s24/9/all

 24/9/1
DIALOG(R)File 155:MEDLINE(R)
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14531642   22040834   PMID: 12044923
  Inhibins/activins as diagnostic markers for ovarian cancer.
  Robertson D M; Stephenson T; Pruysers E; Burger H G; McCloud P; Tsigos A;
Groome N; Mamers P; McNeilage J; Jobling T; Healy D
  Prince Henry's Institute of Medical Research, PO Box 5152, Clayton, Vic.
3168, Australia. david.robertson@med.monash.edu.au
  Molecular and cellular endocrinology (Ireland)  May 31 2002,  191  (1)
 p97-103,  ISSN 0303-7207  Journal Code: 7500844
  Document type: Journal Article; Review; Review, Tutorial
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
  Subfile:  INDEX MEDICUS
  It is widely recognised that the early detection and subsequent
assessment of recurrence of ovarian cancers are key steps for successful
treatment. Available serum markers (e.g. CA125) are sensitive for some
epithelial carcinomas (e.g. serous, endometrioid, clear cell), however,
these markers are less sensitive for granulosa cell tumours and mucinous
carcinomas. Serum inhibin is an ovarian product which decreases to non
detectable levels after menopause , however, certain ovarian cancers
(mucinous carcinomas and sex cord stromal tumours such as granulosa cell
tumours) continue to produce inhibin which provides a basis for a serum
diagnostic test. Studies from this and other laboratories have investigated
the suitability of inhibin as a diagnostic marker by identifying which
inhibin (inhibin A (alphabetaA), inhibin B (alphabetaB), free alpha
subunit) or activin (betaAbetaA) form is associated with these cancers.
Available data show that inhibin assays which detect all inhibin forms,
i.e. assays which detect the alpha subunit both as the free form and as an
alphabeta subunit dimer provide the highest sensitivity/specificity
characteristics as an ovarian cancer diagnostic test. This review will
discuss the data supporting these observations and show recent studies in
which a new alpha subunit monoclonal antibody-based ELISA is used as a
potential diagnostic test. Furthermore, based on the high
sensitivity/specificity characteristics of the respective assays for the
various types of ovarian cancer, the combination of the inhibin assay with
CA125 detects the majority of all ovarian cancers. (46 Refs.)
  Tags: Female; Human; Support, Non-U.S. Gov't
  Descriptors:  *Activins--blood--BL;  *Inhibins--blood--BL;  *Ovarian
Neoplasms--diagnosis--DI;  Antibodies,  Monoclonal  --metabolism--ME;
Follicle Stimulating Hormone--blood--BL; Granulosa Cell Tumor--blood--BL;
 Granulosa Cell Tumor--diagnosis--DI; Ovarian Neoplasms--blood--BL; Protein
Subunits--metabolism--ME; Tumor Markers, Biological--blood--BL
  CAS Registry No.: 0  (Antibodies, Monoclonal); 0  (Protein Subunits); 0
 (Tumor  Markers,  Biological);  104625-48-1  (Activins); 57285-09-3
 (Inhibins); 9002-68-0  (Follicle Stimulating Hormone)
  Record Date Created: 20020604
  Record Date Completed: 20030306
```

24/9/2

DIALOG(R)File 155:MEDLINE(R)

11082931 97438119 PMID: 9293894

MIB-1 expression in breast carcinomas with medullary features. An immunohistological study including correlations with p53 and bcl-2.

Jensen V; Jensen M L; Kiaer H; Andersen J; Melsen F

Institute of Pathology, Aarhus Amtssygehus, Tage Hansensgade, Aarhus C, Denmark.

Virchows Archiv - an international journal of pathology (GERMANY) Aug 1997, 431 (2) p125-30, ISSN 0945-6317 Journal Code: 9423843

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Typical medullary carcinoma (TMC) is usually considered to have a more favourable prognosis than other types of infiltrating breast carcinomas. This is a biological paradox, since its clinical behaviour is not in agreement with its anaplastic morphology and high mitotic rate. It should be remembered that neoplastic growth reflects cell production minus cell loss, the latter being achieved by apoptosis. At present, bcl-2 oncogene (apoptosis inhibitor) and p53 gene are assumed to be involved in the regulation of cell death and tumour proliferation. Sixty breast carcinomas, initially indexed as medullary carcinomas, were re-classified using the diagnostic criteria given by Ridolfi. This **review** yielded 13 typical (TMC), 24 atypical (AMC), and 23 non-medullary carcinomas (NMC). Following antigen retrieval by microwave treatment, immunohistochemical analyses, using MIB-1, p53 and bcl-2 **monoclonal** antibodies were performed on serial sections from formalin-fixed, paraffin-embedded specimens. TMC revealed the highest incidence of intense p53 positivity, and the highest mean MIB-1 index, and absence of the apoptosis-inhibitor protein bcl-2. These results suggest the presence of a higher overall cell turnover in TMC than in AMC and NMC. Increased apoptosis balancing the increased cell proliferation might be among the possible explanations for the more favourable prognosis in TMC.

Tags: Female; Human

Descriptors: *Breast Neoplasms--metabolism--ME; *Carcinoma, Medullary --metabolism--ME; *Nuclear Proteins--metabolism--ME; *Protein p53 --metabolism--ME; *Proto-Oncogene Proteins c-bcl-2--metabolism--ME; Adult; Aged; Aged, 80 and over; Antibodies, **Monoclonal** ; Antigens, Nuclear; Biological Markers--analysis--AN; Breast Neoplasms--pathology--PA; Carcinoma, Medullary--pathology--PA; Immunohistochemistry; **Menopause** ; Middle Age

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Antigens, Nuclear); 0 (Biological Markers); 0 (Nuclear Proteins); 0 (Protein p53); 0 (Proto-Oncogene Proteins c-bcl-2)

Record Date Created: 19971001

Record Date Completed: 19971001

24/9/3

DIALOG(R)File 155:MEDLINE(R)

10697360 97046606 PMID: 8891527

Interest of epitopic dissection in immunoanalysis of proteins and peptides: review of theoretical and practical aspects.

Niccoli P; Ferrand V; Lejeune P J; Carayon P

Laboratoire de Biochimie Endocrinienne et Metabolique, Institut National de la Sante et de la Recherche Medicale, Faculte de Medecine, Marseille, France.

European journal of clinical chemistry and clinical biochemistry - journal of the Forum of European Clinical Chemistry Societies (GERMANY) Sep 1996, 34 (9) p741-8, ISSN 0939-4974 Journal Code: 9105775

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

The literature abounds with reports showing discrepancies in immunoassays of proteins and peptides. Whereas the isomorphism and polymorphism of proteins remains largely hidden in immunoassays making use of polyclonal antibodies, the use of **monoclonal** antibodies uncovered the difficulty of accurately assaying microheterogeneous analytes. Indeed, most proteic hormones are not entities with unique structures but rather mixtures of molecular forms with slight differences in structure which may reflect large variations in biological and immunological activities; the **monoclonal** antibodies appeared clearly less suited than the polyclonal for testing a mixture of isoforms. Protein microheterogeneity also has an impact on assay standardisation, since reference preparations may contain several isoforms of the analyte. Using recombinant glycoprotein does not solve the problem. Regarding the problem of discrepancy in immunoanalysis of proteins and peptides, we could establish, in a previous work, that discrepancy among lutropin assay kits may be related to various causes: i) differences in standard preparation and calibration curves; ii) microheterogeneity of lutropin molecules leading to missing some isoforms due to the restricted epitopic specificity of the **monoclonal** antibodies used in the kits. The epitopic dissection we engaged in appeared thus instrumental in explaining these discrepancies. It allowed us to enumerate epitopes on the surface of lutropin molecules, to elucidate the immunological structure and, finally, to characterize **monoclonal** antibodies used in commercially available lutropin assay kits with regard to their epitopic specificity. This work allowed us to interpret the discrepancy in serum lutropin concentration which was related to the use of **monoclonal** antibody with given specificity. Epitopic dissection may thus be instrumental in explaining discrepancy among immunoassays of proteins and peptides and in improving the accuracy of kits. (19 Refs.)

Tags: Female; Human; Male; Support, Non-U.S. Gov't

Descriptors: *Epitopes--chemistry--CH; *Immunoassay--methods--MT; *Peptides--chemistry--CH; *Proteins--chemistry--CH; Antibodies, **Monoclonal**; Kidney Failure--blood--BL; Luteinizing Hormone--blood--BL; **Menopause**--blood--BL; Polycystic Ovary Syndrome--blood--BL; Polymorphism (Genetics); Reagent Kits, Diagnostic--standards--ST; Reference Values

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Epitopes); 0 (Peptides); 0 (Proteins); 0 (Reagent Kits, Diagnostic); 9002-67-9 (Luteinizing Hormone)

Record Date Created: 19970206
Record Date Completed: 19970206

24/9/4

DIALOG(R)File 155:MEDLINE(R)

10679964 97029114 PMID: 8875126

In vitro fertilisation. A review of drug therapy and clinical management.

Jennings J C; Moreland K; Peterson C M
Department of Pharmacy Practice, University of Utah College of Pharmacy, Salt Lake City, USA.

Drugs (NEW ZEALAND) Sep 1996, 52 (3) p313-43, ISSN 0012-6667
Journal Code: 7600076
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Since the first in vitro fertilisation (IVF) pregnancy was delivered in 1978, this procedure has resulted in thousands of pregnancies and opened a vast new frontier of research and treatment for the infertile couple. Pregnancy rates with IVF improve as the number of high quality embryos available for transfer increases; therefore, ovarian stimulation agents to produce multiple oocysts for IVF are advantageous. Clomifene (clomiphene citrate), human **menopausal** gonadotrophin (hMG; menotropins), and subsequent generations of products are commonly used as stimulation agents.

In conjunction with the stimulation agents, gonadotrophin-releasing hormone (GnRH) agonists and human chorionic gonadotrophin (hCG) serve as adjuvants for successful control of all events in the induction process. Clomifene, an estrogen agonists/antagonist, occupies the estrogen receptor for a longer period of time than estrogen (weeks versus hours). Because this signal is interpreted as low estrogen, GnRH is released, which produces a rise in circulating levels of follicle-stimulating hormone (FSH) and luteinising hormone (LH) and subsequent ovarian follicular development. Menotropins is collected by passing urine from **menopausal** donors over a Sepharose column, followed by removal of high molecular weight impurities by chromatography. The mixture of FSH and LH is biologically standardised. This product stimulates multiple ovarian follicular development. Urofollitrophin is produced using antibodies to hCG anchored to a separation column. LH then can be excluded from the eluate by binding to the hCG antibodies (LH immunoaffinity column). Highly purified FSH is obtained by passing **menopausal** urine over a column with **monoclonal** antibodies to FSH. The isolated FSH is then eluted from the column by a highly basic solution and crystallised. This product delivers FSH at a 90% purity and can be administered subcutaneously rather than intramuscularly. Dosage is standardised on a mg/kg basis. Recombinant human FSH is completely free of LH and offers the advantages of better batch consistency, greater purity, and absence of any human contaminants. It may be given both subcutaneously and intravenously. Genetically engineered FSH combines portions of the native protein with another protein (hCG) which enhances its potency and extends the half-life compared with wild-type FSH. Short, medium and ultra-long activity analogues of genetically engineered FSH may be used to tailor stimulation protocols in various clinical situations. Growth hormone is an adjuvant to ovarian stimulation which results in a decreased number of ampoules of menotropins being required to achieve ovulation in poor responders. Ovulation triggers include both hCG and GnRH agonists. Progesterone supplementation is generally used in the luteal phase of the IVF cycle and is administered by intramuscular injection or vaginal suppository. It appears that conscious sedation with midazolam, pethidine (meperidine) and fentanyl is nontoxic for oocyte recovery. If full anaesthesia is required for gamete intrafallopian tube transfer (GIFT) or zygote intrafallopian tube transfer (ZIFT), balanced anaesthesia with nitrous oxide and an opioid appears to be the most appealing option. Appropriate information on the clinical use of the drugs used in IVF greatly reduces patient stress associated with the complex multidrug regimens associated with the procedure. (180 Refs.)

Tags: Female; Human

Descriptors: *Fertilization in Vitro--methods--MT; *Reproductive Techniques; Antibiotic Prophylaxis; Chorionic Gonadotropin--administration and dosage--AD; Clomiphene--administration and dosage--AD; Clomiphene --adverse effects--AE; Embryo Transfer; Gonadorelin--agonists--AG; Gonadorelin--antagonists and inhibitors--AI; Menotropins--administration and dosage--AD; Menotropins--adverse effects--AE; Oocyte Donation; Ovulation--drug effects--DE; Ovulation Induction

CAS Registry No.: 0 (Chorionic Gonadotropin); 33515-09-2 (Gonadorelin) ; 61489-71-2 (Menotropins); 911-45-5 (Clomiphene)

Record Date Created: 19970124

Record Date Completed: 19970124

24/9/5

DIALOG(R)File 155:MEDLINE(R)

06801833 91041517 PMID: 2233116

[Pathophysiology of atherosclerosis. II. Etiopathogenic mechanisms and risk factors]

Patofiziologija ateroskleroze. II. Etiopatogenetski mehanizmi i faktori rizika.

Reiner Z; Tedeschi-Reiner E

Medicinskog fakulteta Sveucilista u Zagrebu, Klinickog odjela Zavoda za opcu patolosku fiziologiju KBC Rebro.

Lijecnicki vjesnik (YUGOSLAVIA) May-Jun 1990, 112 (5-6) p175-82, ISSN 0024-3477 Journal Code: 0074253

Document type: Journal Article; Review; Review, Academic ; English

Abstract
Languages: SERBO-CROATIAN (ROMAN)
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
The authors present an up-to-date **review** on etiopathogenesis of atherosclerosis. Theories of etiology of atherosclerosis are described: response-to-injury hypothesis, lipid deposition hypothesis, lysosome hypothesis, encrustation hypothesis, mural thrombi hypothesis, **monoclonal** and clonal senescence hypothesis. The role of endothelial injury and platelet adhesion as well as smooth muscle cells proliferation due to these events, their growth control and the role of macrophages in atherogenesis are explained thoroughly. Special attention is focused on the interaction of arterial cells and lipoproteins at sites of vessel injury, lipid metabolism of the lesion and on synergy of arterial injury caused by various injury mechanisms and hypercholesterolemia in atherogenesis. Atherosclerotic risk factors and their impact on atherogenesis are discussed as well (e.g. hyperlipoproteinemia, hypertension, tobacco smoking, diabetes and abnormal glucose tolerance, gout, obesity, **menopause** and oral contraceptives, diminished physical activity, type A of personality behavior etc.). The possibilities of regression or reversal of ateromatous plaques are presented too. (121 Refs.)
Tags: Animal; Human
Descriptors: *Arteriosclerosis--etiology--ET; Arteriosclerosis--physiopathology--PP; Risk Factors
Record Date Created: 19901212
Record Date Completed: 19901212

24/9/6
DIALOG(R)File 155:MEDLINE(R)

05726845 88080240 PMID: 3319146
Passive, adoptive, and active immunotherapy: a review of clinical trials in cancer.
Mathe G
Service des Maladies Sanguines et Tumorales and ICIG (Univ. Paris-Sud, CNRS UA 04-1163, Villejuif, France.
Cancer detection and prevention. Supplement - official publication of the International Society for Preventive Oncology, Inc (UNITED STATES) 1987, 1 p279-90, ISSN 1043-6995 Journal Code: 8808253
Document type: Clinical Trial; Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
The results today of passive immunotherapy with **monoclonal** antibodies (MAb) are still very limited, even via its indirect methods (in vitro tumor cell clearance of bone marrow before autologous retransplantation, transport of cytostatic chemicals, and radiation). Tumor cell heterogeneity requires the use of several MAb. Adoptive immunotherapy in the form of the graft vs leukemia (GVL) reaction associated with the graft vs host (GVH) reaction, after an allogeneic bone marrow transplantation, first demonstrated in animals in 1962, has been confirmed in man. The material and operational development of tumor immunology, immunopharmacology, and clinical trial methodology should improve active immunotherapy results and help to convert into a cure what is often a significant but only marginal increase: 1) of disease-free survival or 2) of survival or 3) of survival after relapse. The general ineffective management and use of adjuvant chemotherapy for all tumors except breast carcinoma before **menopause** will, on the other hand, contribute to necessary new concepts of how to manage the postremission, residual, minimal disease. (112 Refs.)
Tags: Comparative Study; Human
Descriptors: *Immunity, Active; *Immunization, Passive; *Immunotherapy; *Neoplasms--therapy--TH; Clinical Trials
Record Date Created: 19880224
Record Date Completed: 19880224
?logoff hold

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      04jun03 16:48:34 User228206 Session D1981.4
           $5.77    1.804 DialUnits File155
              $1.26  6 Type(s) in Format  9
           $1.26  6 Types
     $7.03  Estimated cost File155
     $0.92  TELNET
     $7.95  Estimated cost this search
     $7.95  Estimated total session cost   1.804 DialUnits


### Status: Signed Off. (4 minutes)

### Status: Path 1 of [Dialog Information Services via Modem]

### Status: Initializing TCP/IP using (UseTelnetProto 1 ServiceID pto-dialog)
Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ******** HHHHHHHH SSSSSSSS?
### Status: Signing onto Dialog
 ********
ENTER PASSWORD:
 ******** HHHHHHHH SSSSSSSS? ********
Welcome to DIALOG
### Status: Connected

Dialog level 02.14.01D

Reconnected in file 155 04jun03 16:52:17
* * * * See HELP NEWS 225 for information on new search prefixes
and display codes

***                                    ***


File 155:MEDLINE(R)  1966-2003/Jun W1
       (c) format only 2003 The Dialog Corp.
*File 155: Medline has been reloaded and accession numbers have
changed.  Please see HELP NEWS 155.

      Set  Items  Description
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Cost is in DialUnits
?ds

Set     Items   Description
S1      54849   GONADOTROP?
S2      26212   R1-R2
S3      87343   R1-R18
S4     110136   (S1 OR S2 OR S3)
S5        733   S4 AND ISOFORM?
S6        310   S5 AND (DISTING? OR DIFFERENTI? OR IDENTIF? OR SEPARA? OR -
                MENOPAUS?)
S7        109   S6 AND (ASSAY? OR IMMUNOASSAY? OR EIA OR ELISA OR ELIZA OR
                METHOD?)
S8         34   S7/2000:2003
S9         75   S7 NOT S8
S10        11   S9 AND (HYBRIDOM? OR MONOCLONAL?)
S11       263   S5/2000:2003
S12       470   S5 NOT S11
S13        27   S12 AND SIAL?
S14        27   S13 NOT S10
S15     26323   MENOPAUS?
S16    312426   REVIEW OR TUTOR?
S17      1089   S15 AND S16
S18       118   S17 AND (GONAD? OR FSH? OR LH?)
```

```
S19        114   S18 AND HUMAN?
S20         52   S19 AND (DETERMIN? OR MEASUR? OR DISTING? OR DIFFERENT? OR
                 ANALYZ?)
S21          0   S20 AND ISOFORM?
S22         53   S17 AND PREDICT?
S23          0   S22 AND MONOCLONAL?
S24          6   S17 AND MONOCLONAL?
?s (sialic? or sialyl?) (25n) (moab or mab or monoclonal or antibod?)
            13686  SIALIC?
             6338  SIALYL?
             3361  MOAB
            24387  MAB
           167453  MONOCLONAL
           620233  ANTIBOD?
      S25    1536  (SIALIC? OR SIALYL?) (25N) (MOAB OR MAB OR MONOCLONAL OR
                   ANTIBOD?)
?s s25 and s15
             1536  S25
            26323  S15
      S26       1  S25 AND S15
?t s26/9/all

 26/9/1
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

07836627   93292255   PMID: 7685676
  The role of tumor markers in the preoperative diagnosis of ovarian cysts.
  Schwartz P E
  Department of Obstetrics and Gynecology, Yale University School of
Medicine, New Haven, CT 06510.
  Clinical obstetrics and gynecology (UNITED STATES)  Jun 1993, 36 (2)
 p384-94, ISSN 0009-9201  Journal Code: 0070014
  Document type: Journal Article; Review; Review, Tutorial
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
  Subfile:   INDEX MEDICUS
  (37 Refs.)
  Tags: Female; Human
  Descriptors: *Ovarian Cysts--diagnosis--DI; *Preoperative Care; *Tumor
Markers, Biological--analysis--AN; Adult; Annexin V--analysis--AN;
Antibodies, Monoclonal; Antigens, Neoplasm--analysis--AN; Antigens, Surface
--analysis--AN; Antigens, Tumor-Associated, Carbohydrate--analysis--AN;
Antigens, Viral--analysis--AN; Glycoproteins--analysis--AN; Gonadotropins
--urine--UR; Interleukin-6--analysis--AN; Lipids--analysis--AN; Macrophage
Colony-Stimulating Factor--analysis--AN; Menopause ; Middle Age; Ovarian
Cysts--chemistry--CH; Ovarian Cysts--urine--UR; Peptides--analysis--AN;
Sialic Acids--analysis--AN; Tissue Polypeptide Antigen; alpha-Fetoproteins
--analysis--AN
  CAS Registry No.: 0 (Annexin V); 0 (Antibodies, Monoclonal); 0
 (Antigens, Neoplasm); 0 (Antigens, Surface); 0 (Antigens,
Tumor-Associated, Carbohydrate); 0 (Antigens, Viral); 0 (Glycoproteins)
; 0 (Gonadotropins); 0 (Interleukin-6); 0 (Lipids); 0 (Peptides); 0
 (Sialic Acids); 0 (Tissue Polypeptide Antigen); 0 (Tumor Markers,
Biological); 0 (alpha-Fetoproteins); 0 (cytomegalovirus early antigens)
; 0 (lipid-associated sialic acid); 0 (ovarian tumor associated antigen)
; 0 (sialosyl-Tn antigen); 81627-83-0 (Macrophage Colony-Stimulating
Factor)
  Record Date Created: 19930720
  Record Date Completed: 19930720
?logoff hold
       04jun03 16:52:34 User228206 Session D1981.5
            $1.37    0.427 DialUnits File155
               $0.21  1 Type(s) in Format  9
            $0.21  1 Types
     $1.58  Estimated cost File155
     $0.22  TELNET
     $1.80  Estimated cost this search
```

```
     $1.80  Estimated total session cost   0.427 DialUnits


### Status: Signed Off. (1 minutes)

### Status: Path 1 of [Dialog Information Services via Modem]

### Status: Initializing TCP/IP using (UseTelnetProto 1 ServiceID pto-dialog)
Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ******** HHHHHHHH SSSSSSSS?
### Status: Signing onto Dialog
 ********
ENTER PASSWORD:
 ******** HHHHHHHH SSSSSSSS? ********
Welcome to DIALOG
### Status: Connected


Dialog level 02.14.01D

Reconnected in file 155 04jun03 16:53:23
* * * * See HELP NEWS 225 for information on new search prefixes
and display codes

***                                    ***


File 155:MEDLINE(R)  1966-2003/Jun W1
       (c) format only 2003 The Dialog Corp.
*File 155: Medline has been reloaded and accession numbers have
changed.  Please see HELP NEWS 155.

      Set  Items  Description
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Cost is in DialUnits
?s s25 and (premenopaus? or postmenopaus?)
            1536  S25
            8052  PREMENOPAUS?
           22771  POSTMENOPAUS?
     S27       0  S25 AND (PREMENOPAUS? OR POSTMENOPAUS?)
?ds

Set     Items   Description
S1      54849   GONADOTROP?
S2      26212   R1-R2
S3      87343   R1-R18
S4     110136   (S1 OR S2 OR S3)
S5        733   S4 AND ISOFORM?
S6        310   S5 AND (DISTING? OR DIFFERENTI? OR IDENTIF? OR SEPARA? OR -
                MENOPAUS?)
S7        109   S6 AND (ASSAY? OR IMMUNOASSAY? OR EIA OR ELISA OR ELIZA OR
                METHOD?)
S8         34   S7/2000:2003
S9         75   S7 NOT S8
S10        11   S9 AND (HYBRIDOM? OR MONOCLONAL?)
S11       263   S5/2000:2003
S12       470   S5 NOT S11
S13        27   S12 AND SIAL?
S14        27   S13 NOT S10
S15     26323   MENOPAUS?
S16    312426   REVIEW OR TUTOR?
S17      1089   S15 AND S16
S18       118   S17 AND (GONAD? OR FSH? OR LH?)
S19       114   S18 AND HUMAN?
S20        52   S19 AND (DETERMIN? OR MEASUR? OR DISTING? OR DIFFERENT? OR
```

```
             ANALYZ?)
S21          0   S20 AND ISOFORM?
S22         53   S17 AND PREDICT?
S23          0   S22 AND MONOCLONAL?
S24          6   S17 AND MONOCLONAL?
S25       1536   (SIALIC? OR SIALYL?) (25N) (MOAB OR MAB OR MONOCLONAL OR A-
             NTIBOD?)
S26          1   S25 AND S15
S27          0   S25 AND (PREMENOPAUS? OR POSTMENOPAUS?)
?s s15 (10n) sial?
           26323  S15
           29610  SIAL?
     S28       5  S15 (10N) SIAL?
?t s28/9/all

 28/9/1
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
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11540941 98432264 PMID: 9761120

Osteopontin expression in a group of lymph node negative breast cancer patients.

Tuck A B; O'Malley F P; Singhal H; Harris J F; Tonkin K S; Kerkvliet N; Saad Z; Doig G S; Chambers A F

London Regional Cancer Centre, London Health Sciences Centre, Department of Pathology, University of Western Ontario, Canada. atuck@julian.uwo.ca

International journal of cancer. Journal international du cancer (UNITED STATES) Oct 23 1998, 79 (5) p502-8, ISSN 0020-7136 Journal Code: 0042124

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The aim of this study was to examine the cellular distribution of osteopontin (OPN) protein [by immunohistochemical (IHC) analysis] and mRNA [by in situ hybridization (ISH)] in the primary tumors of lymph node negative (LNN) breast cancer patients and to determine whether the level of immunodetectable OPN may be associated with tumor aggressiveness. We examined OPN levels in tumors from 154 patients with LNN breast cancer who were followed for a median of 7 years (range 1.7-16.3 years). IHC staining for OPN was seen in tumor infiltrating macrophages and lymphocytes in 70% of these tumors, and in the carcinoma cells themselves in 26%. ISH was performed to determine cellular distribution of OPN mRNA expression in sections from selected tumors. OPN mRNA was detected in groups of tumor cells, individual tumor cells and tumor infiltrating macrophages and lymphocytes. Matched sections showed that some tumor cells with IHC staining for OPN protein were also positive for OPN mRNA by ISH, in contrast with previous studies which have shown OPN mRNA expression only in tumor infiltrating inflammatory cells. Our results thus indicate that OPN protein can be produced by breast cancer cells in vivo and suggest that it may also be taken up from the environment (i.e., secreted by inflammatory cells or other tumor cells). Tumor cell IHC staining intensity was then assessed using a semiquantitative scoring system. Univariate analysis showed tumor cell OPN positivity above an optimized cutpoint to be significantly associated with decreased disease-free survival (DFS) and overall survival (OS). The results of this pilot study thus suggest that the ability of breast cancer cells to either synthesize OPN or to bind and sequester OPN from the microenvironment may be associated with tumor aggressiveness and poor prognosis.

Tags: Female; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.

Descriptors: *Breast Neoplasms--chemistry--CH; *Gene Expression; *Lymph Nodes--pathology--PA; *Sialoglycoproteins--analysis--AN; Adult; Aged; Aged, 80 and over; Breast Neoplasms--pathology--PA; Disease-Free Survival; Immunohistochemistry; In Situ Hybridization; **Menopause** ; Middle Age; Prognosis; RNA, Messenger--analysis--AN; **Sialoglycoproteins** --genetics--GE

CAS Registry No.: 0 (RNA, Messenger); 0 (Sialoglycoproteins); 106441-73-0 (osteopontin)

Record Date Created: 19981015
Record Date Completed: 19981015

28/9/2
DIALOG(R)File 155:MEDLINE(R)

11264213 98142571 PMID: 9481572
The relationship between the female menopause **and serum** sialic **acid, a known cardiovascular risk factor.**
Crook M; Collins D; Lumb P; Fogelman I; Treloar A
Dept Chemical Pathology, Guy's Hospital, London, UK.
European journal of obstetrics, gynecology, and reproductive biology (IRELAND) Feb 1998, 76 (2) p185-7, ISSN 0301-2115 Journal Code: 0375672
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Serum total sialic acid (SA) has recently been reported as a cardiovascular risk factor. The risk of cardiovascular disease increases after the menopause in females. However, there are little data looking at the relationship between serum SA and the menopause. Overall 92 females were studied. The women were divided into five groups: the first three groups were age-matched pre-menopausal (n = 20), peri-menopausal (n = 10) and post-menopausal women (n = 20). In order to study serum SA changes with adult female age we also studied 14 young pre-menopausal women and 28 elderly women. There was no significance difference between the serum SA concentration in the age-matched pre-, peri- or post-menopausal women (62.7 +/- 10.4 mg/dl, 61.7 +/- 4.5 mg/dl, 62.9 +/- 7.0 mg/dl respectively). Furthermore, there was no significant difference between the serum SA in the "young" women (64.7 +/- 9.8 mg/dl) and that of the peri-, pre- or post-menopausal women. However, in the elderly women the serum SA was elevated (75.6 +/- 16.6 mg/dl) with P < 0.05 for each comparison group. In conclusion, serum SA does not seem to change at the time of the female menopause although in elderly women (average age 75.6 +/- 16.6 years) it increases. The reason for this increase is not known and may merit further research.
Tags: Female; Human
Descriptors: *Cardiovascular Diseases--blood--BL; *Menopause--physiology --PH; *N-Acetylneuraminic Acid--blood--BL; Adolescent; Adult; Aged; Aged, 80 and over; Middle Age; Reference Values; Risk Factors
CAS Registry No.: 131-48-6 (N-Acetylneuraminic Acid)
Record Date Created: 19980326
Record Date Completed: 19980326

28/9/3
DIALOG(R)File 155:MEDLINE(R)

10919445 97271577 PMID: 9126503
Serum sialic acid and its correlates in community samples from Akita, Japan and Minneapolis, USA.
Lindberg G; Iso H; Rastam L; Lundblad A; Folsom A R
NEPI Foundation, Medical Research Centre, Malmo University Hospital, Sweden.
International journal of epidemiology (ENGLAND) Feb 1997, 26 (1) p58-63, ISSN 0300-5771 Journal Code: 7802871
Contract/Grant No.: N01-HC-55109; HC; NHLBI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
OBJECTIVE: The concentration of serum total sialic acid (S-TSA) is one recently investigated risk marker for cardiovascular mortality and

atherosclerosis. Since the mortality from coronary heart disease is higher in the United States than in Japan, one could expect the S-TSA to be higher among Caucasian US citizens than among Japanese citizens, a hypothesis that is tested in this study. DESIGN: Cross-sectional study of population-based samples of Japanese and US Caucasian men and women. SETTING: The rural community Akita, Japan, and the suburbs of Minneapolis, Minnesota. SUBJECTS: These were 75 consecutive men and women from Akita and Minneapolis respectively aged 47-69 years in 1990. People who had smoked cigarettes during the past 5 years; who had a history of diabetes mellitus, liver disease, coronary heart disease, or stroke; or who were taking anticoagulants were excluded. OUTCOME MEASURES: Serum total sialic acid levels in male and female Japanese and US Caucasian subjects with adjustment for age, systolic blood pressure, fibrinogen, triglycerides and in women also for **menopausal** status. Race and sex-specific correlations with serum total **sialic** acid for selected cardiovascular risk markers. RESULTS: The entire sialic acid distributions were shifted to the right in Caucasian men and women compared to Japanese men and women. The mean +/- standard deviation concentrations of S-TSA were 54.1 +/- 5.3 mg/dl in Japanese men and 58.7 +/- 5.6 mg/dl in Caucasian men ($P < 0.001$). In women, the concentrations were 54.8 +/- 5.1 and 63.1 +/- 6.0 mg/dl respectively ($P < 0.001$). S-TSA level correlated significantly and positively with fibrinogen levels in Caucasian and Japanese men and women and with triglyceride levels in Caucasian and Japanese men and in Caucasian women but not in Japanese women. After adjustment for age, systolic blood pressure, fibrinogen, triglycerides and **menopausal** status, the **sialic** acid levels were 2.2 ($P = 0.009$) and 6.2 ($P < 0.001$) mg/dl higher in Caucasian compared to Japanese men and women respectively. CONCLUSIONS: Higher S-TSA levels in Caucasians living in Minneapolis compared to Japanese living in Akita, Japan is in concordance with the higher cardiovascular mortality in the US. Differences in S-TSA levels may reflect international differences in the prevalence of atherosclerosis.

Tags: Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Descriptors: *Coronary Arteriosclerosis--blood--BL; *Coronary Arteriosclerosis--epidemiology--EP; *N-Acetylneuraminic Acid--blood--BL; Aged; Biological Markers--analysis--AN; Biological Markers--blood--BL; Coronary Arteriosclerosis--diagnosis--DI; Cross-Sectional Studies; Incidence; Japan--epidemiology--EP; Middle Age; Minnesota--epidemiology--EP; Probability; Risk Factors; Rural Population; Sampling Studies; Sensitivity and Specificity; Survival Rate

CAS Registry No.: 0 (Biological Markers); 131-48-6 (N-Acetylneuraminic Acid)

Record Date Created: 19970521

Record Date Completed: 19970521

28/9/4

DIALOG(R)File 155:MEDLINE(R)

03379462 81070089 PMID: 7440702

Difference in glycosylation between secreted and pituitary free alpha-subunit of the glycoprotein hormones.

Kourides I A; Hoffman B J; Landon M B

Journal of clinical endocrinology and metabolism (UNITED STATES) Dec 1980, 51 (6) p1372-7, ISSN 0021-972X Journal Code: 0375362

Contract/Grant No.: AM-00679; AM; NIADDK; CA-08748; CA; NCI; CA-23185; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

Tags: Comparative Study; Female; Human; Male; Support, U.S. Gov't, P.H.S.

Descriptors: *Peptide Fragments--metabolism--ME; *Pituitary Gland--metabolism--ME; *Thyrotropin--metabolism--ME; Adult; Carcinoid Tumor--metabolism--ME; Chemistry; Galactose--metabolism--ME; Kidney Failure, Chronic--metabolism--ME; **Menopause** ; Middle Age; Molecular Weight; Pituitary Neoplasms--metabolism--ME; **Sialic** Acids--metabolism--ME;

Thyrotropin--blood--BL
CAS Registry No.: 0 (Peptide Fragments); 0 (Sialic Acids); 26566-61-0 (Galactose); 9002-71-5 (Thyrotropin)
Record Date Created: 19810219
Record Date Completed: 19810219

28/9/5
DIALOG(R)File 155:MEDLINE(R)

02305700 76269879 PMID: 183223
Serum sialic acid levels in lung cancer patients.
Krolikowski F J; Reuter K; Waalkes T P; Sieber S M; Adamson R H
Pharmacology (SWITZERLAND) 1976, 14 (1) p47-51, ISSN 0031-7012
Journal Code: 0152016
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
The levels of N-acetyl neuraminic acid (**sialic** acid) in normal men and pre-and post- **menopausal** women were determined. Smoking post- **menopausal** estrogen therapy, oral contraceptives, and refreezing had no effects on **sialic** acid levels. Pre-treatment values from patients with lung carcinoma showed markedly elevated levels of sialic acid (0.697 +/- 0.149 muM/ml) as compared to those from normal controls (0.432 +/- 0.067 muM/ml). The potential usefulness of sialic acid as a biological marker is discussed.
Tags: Female; Human
Descriptors: *Adenocarcinoma--blood--BL; *Carcinoma, Small Cell--blood--BL; *Carcinoma, Squamous Cell--blood--BL; *Lung Neoplasms--blood--BL; *Sialic Acids--blood--BL; Smoking
CAS Registry No.: 0 (Sialic Acids)
Record Date Created: 19761101
Record Date Completed: 19761101
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$1.05 5 Types
$2.27 Estimated cost File155
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Status: Signed Off. (1 minutes)